The epidemiology of infections in blood donors and assessment of the risk of transfusion transmitted infections

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PhD

July 2001

accepted 2002

Abstract

Surveillance of infections in blood donors and blood recipients can be useful for both transfusion medicine and public health. This thesis describes how an enhanced surveillance system for transfusion-transmissible infections has been established in England and Wales.

Data from the surveillance system (1995 to 1999) have been used to monitor test performance and to describe the epidemiology of HBV, HCV and HIV in blood donors. The prevalence and incidence of HBV, HCV and HIV infections in blood donors have been monitored and were generally stable, and low compared to other countries and to other groups in the UK. HCV prevalence decreased throughout the 1990s. The exposure histories reported by infected donors indicate that donor selection largely succeeds in excluding high-risk groups, but also identify some failures in communication of, or compliance with, exclusion criteria.

Diagnosed, reported, post-transfusion infections were rare and after investigation only 20% (21) were shown to have been transmitted by transfusion. The majority (52%) of reported transfusion-transmitted infections, and resulting deaths (3 of 4) were due to bacteria. The number of undiagnosed infections is not known but was estimated for HIV, HBV and HCV by calculations of the probability of infectious donations entering the blood supply due to true or false negatively to tests performed on donations prior to release. Various methods and assumptions have been used to investigate the robustness of these estimates and to develop an appropriate method for ongoing use in England and Wales.

An enhanced surveillance system for transfusion-transmissible infections, that works in collaboration with national surveillance of infectious diseases and of non-infectious complications of transfusion, has been shown – despite some limitations - to provide data and analyses that have aided transfusion medicine and public health in England and Wales. This surveillance continues to develop and improve and further related work is planned.

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Preface

This thesis has been written by Kate Soldan. Where the published work of others is used, or referred to, this is referenced. The work described in this thesis was predominantly designed and conducted by Kate Soldan. The contribution of others to the work described is acknowledged below.

Acknowledgments

For their contributions to the design of the surveillance system and interpretation of the data: - I am very grateful to all members of the NBA/PHLS Joint work Steering group (New name as ad hoc working group reporting to the Advisory Committee on Blood Borne Viruses: "NBA/PHLS CDSC transfusion transmissible infections co-ordinating committee"): Dr Julia Heptonstall (till October 1996), Dr Philip Mortimer, Mrs Janet Mortimer, Dr Ty Pitt, Dr Mary Ramsay and Mr Alan Slopecki for advice and comments on the development and use of the surveillance system.

Particular thanks go to Dr Julia Heptonstall and Dr Mary Ramsay and Dr John Barbara for initiating and supervising the work, and providing good advice whenever needed. And to Andy Hall for supervision of this thesis.

For their contributions to other aspects of the work: - I should like to thank Paddy Farringdon and Nick Andrews for their advise on statistics and for assistance with estimation of credibility intervals in chapter 5, and Nick for writing programmes to conduct statistical analyses of the donation testing data (described in chapter 3). Thanks also to Janet Mortimer and Vicky Gilbart for collaboration in the collation of data about HIV positive donors, to Marion Collins for managing the data used in the survey of acute HBV infections associated with transfusion and to Alison Pottinger, Dawn Appleby, Anne Beckman, and Laura Able for assistance with data entry at the National Blood Authority.

For their collaboration and assistance:- I should like to acknowledge the Welsh Blood Service and the SHOT working group for their helpful collaboration and the CDSC Training Committee for paying my PhD fees. Thanks also go to Dr Angela Robinson for support and for facilitating access to NBS data and resources. Particular thanks go to staff at blood centres and other laboratories who have provided the reports and follow up information necessary for this work.

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CHAPTER 1. THE EPIDEMIOLOGY OF TRANSFUSION TRANSMISSIBLE INFECTIONS IN BLOOD DONORS AND RISKS OF TRANSFUSION TRANSMITTED INFECTIONS - A REVIEW OF THE LITERATURE. 11

1.1 Transfusion transmissible infections

Transfusion of blood collected from one individual into another carries with it the possibility of transmitting blood-borne infectious agents. This is particularly important as patients receiving blood transfusions are often immunosuppressed or otherwise relatively vulnerable to infection. Transmission of syphilis (*Treponema pallidum*) was recognised in the early days of transfusion when blood was transferred directly from donor to recipient. Testing donations for treponemal antibodies and storage of blood between collection and transfusion has overcome this problem. Since then, three viral infections - HBV, HCV, and HIV - have been the predominant transfusion-transmitted agents to cause disease and to prompt changes in transfusion practice. Selective exclusion of individuals from giving blood based on increased risk associated with these blood-borne infections, and the testing of blood donations for serological markers of these infections have greatly reduced the risk of infectious donations entering the blood supply. Nevertheless, some risk will always remain because donor selection and serological testing of donations cannot identify and exclude every infectious donation.

At certain stages in their natural history many viral, bacterial, and protozoal infections can be blood-borne and may be transmitted by transfusion. Fortunately for transfusion medicine, many blood-borne organisms cause symptoms during the period of blood-borne infectivity that render their victims too unwell, or obviously unfit, to donate blood. Other agents are only present in the blood transiently and some agents do not survive the conditions of blood storage outside the human body.

Variations in the length of time for which agents are present in the blood, and viable in stored blood, determine, to a large extent, variations in the risk of infectious donations being collected. Infections of most concern are those that have long periods of infectivity in the absence of any clinical signs or symptoms of infection and are stable in stored blood (for example, HBV, HIV and HCV). The length of time between infection and the development of detectable serological markers (the window period) also varies between agents (for example, 22 days for anti-HIV (Busch MP, 1995) and 66 days for anti-HCV (Barrera JM, 1995) using current assays). During the very start of this period – often referred to as the "eclipse" –infectious agent (nucleic acid) is absent from the blood or only found in very small numbers and blood is unlikely to be infectious if transfused. The infectious window period is therefore shorter than the total window period. The shorter the infectious window period, relative to the total asymptomatic sero-positive infective period, the better is the detection of infectious donations by serological testing.

For infections with transient blood-borne infectivity (for example, HAV and parvovirus B19), the risk of infectious donations being collected depends upon the incidence of the infection in the donor population and the length of the infectious period.

This general pattern of markers of infection can not be assumed for all infectious agents, as has been recently found for the infectious agents that cause spongiform encephalopathies (e.g. BSE, CJD). These agents do not conform in a number of ways, for example they do not contain nucleic acids.

Viral infections

Donor selection and donation testing prevent HBV, HCV and HIV infectious donations from entering the blood supply. However, these

interventions are not 100% effective and transmissions of HBV (Elghouzzi M-H, 1995), HCV (Kitchen AD, 1996; Vrielink H, 1995) and HIV (Conley LJ, 1992; Mak RP, 1993; Crawford RJ, 1987; CDR Weekly, 1997) by blood that tested negative for markers of infection have been documented in the UK and elsewhere. The expected risk of infectious donations entering the blood supply has also been estimated (Lackritz EM, 1995; Schreiber GB, 1996; Courouce AM, 1996). The potential of most other known blood borne viruses to be transmitted by transfusion and to cause morbidity or mortality in recipients is limited by relatively short periods of viraemia, and therefore low prevalence in donations, and by high immunity in recipients and low frequency of disease associated with infection. These factors, probably along with some transmissions resulting in mild, or non-specific symptomatology that is not precisely diagnosed, account for the rarity of clinically apparent HAV, parvo virus B19, CMV or EBV infection associated with transfusion. The case for intervention against transfusion transmission of HTLVI & II infections has become more compelling as reports of disease associated with these viruses, and particularly of disease in transfusion recipients (who are often immunosuppressed), have increased. (HTLV I is the etiological agent of adult T-cell leukaemia/lymphoma and of tropical spastic paraparesis or human T-cell lymphotropic virus type I-associated myelopathy (Ferreira OC, 1997). HTLV II is thought to cause a neurological syndrome similar to HTLV-I associated myelopathy and there is some evidence suggesting HTLV II predisposes to skin and soft tissue bacterial infections in injecting drug users (Murphy EL, 1996).)

Box 1. Examples of viral infectious agents that have the potential for transmission by blood transfusion.
(Adapted from Barbara JAJ, 1994)

Hepatitis viruses

Hepatitis A (HAV) - no carrier state (rarely transmitted)

Hepatitis B (HBV) - carrier state

Hepatitis D (HDV, or delta virus) - requires HBV

Hepatitis C (HCV) - carrier state

Human retroviruses

Human immunodeficiency viruses, HIV-1 & 2 - latent state

Human T-cell leukaemia, HTLV-I & II - latent state

Herpes viruses

Cytomegalovirus (CMV) - latent state

Epstein-Barr virus (EBV) - latent state

Non-viral infections

Potentially, a large number and variety of non-viral agents may be transmitted by transfusion, both endogenous agents present in the donor at the time of donation and exogenous contamination occurring during collection and processing. The transmission of syphilis was a serious problem with early transfusions given directly from donor to patient. The storage of certain blood components (e.g. platelets) at 22°C rather than 4°C provides more favourable growth conditions for bacteria. Although rare, serious sequelae such as septicaemia and septic shock do occur (e.g. Boulton F, 1997) and approaches to identify and reduce the risks are under consideration.

Box 2. Examples of non-viral infectious agents that have the potential for transmission by blood transfusion.
(From Kitchen AD, 1994)

Bacteria

Endogenous bacteria

Syphilis (*Treponema pallidum*)

Lyme disease (*Borrelia burgdorferi*)

Brucellosis (*Brucella melitensis*)

Yersinia entercolitica (and others)

Exogenous bacteria

Environmental species, for example *Staphylococcus epidermidis*, *Pseudomonas* spp. and *Serratia marcescens*

Rickettsiae

Rocky mountain spotted fever (*Rickettsia rickettsii*)

Q fever (*Coxiella burnettii*)

Parasites

Malaria (*Plasmodium* spp.)

Toxoplasmosis (*Toxoplasma gondii*)

Trypanosomiasis (Chagas' disease and sleeping sickness)

Whether prion disease can be transmitted by transfusion is currently uncertain (Ricketts MN, 1997). Unknown infections and infections with increasing potential to cause harm to recipients due to the changing epidemiology of the infection, or changing vulnerability of blood recipients to disease, may pose the greatest risks of infection to recipients. Avoidance of unnecessary transfusion and vigilance of blood-borne infectious diseases in the general population and in blood recipients are therefore important general components of transfusion medicine. Vigilance of infectious diseases in blood recipients – particularly in multiply transfused patients - can also contribute to early public health knowledge of emerging infections and to their control.

Strategies to reduce risk

There are three main strategies for preventing infectious donations from entering the blood supply issued to hospitals. The first concerns the recruitment and selection of blood donors who do not have a known increased risk of infection. The second is the testing of donations for markers of infections. The third covers the control of cleanliness during component production.

Selection of blood donors

Donor recruitment and selection aims to select a group of individuals with a low risk of infection. To achieve this low risk both the prevalence of infection and the incidence of infection should be low. In practice incidence is often difficult to measure. The selection of a "low risk" group therefore often depends on identifying groups with low seroprevalence and without the characteristics or exposures associated with an increased risk of infection. There are some general guidelines for donor selection (which are well founded in experience). Voluntary donors are considered safer than paid donors, and repeat donors safer than new donors. However, selection of these individuals is not guaranteed to be effective - particularly for newly identified infections or for infections with changing epidemiology.

New knowledge about exposures of increased risk for blood-borne infections is regularly considered so that guidelines for pre-donation donor selection in the UK can be revised as necessary. Unapparent infections and non-recognition or denial of risk factors in donors prevents the exclusion of all infected donations by pre-donation selection criteria.

Donation testing

A pre-transfusion test for syphilis has been performed routinely on each blood donation since the beginning of the transfusion service in England and Wales in 1946. It has been known since 1941 that spirochaetes survive poorly at low temperatures (Turner TB, 1941) and the storage of blood at 4-6°C has largely eliminated syphilis transmission by transfusion. There is no mandatory requirement for testing in Europe and the need for testing is now a matter for debate. The most persuasive arguments for continuing have been the increasing use of products such as platelets that are stored at 22°C and the

expectation that testing for syphilis may exclude some individuals who may be at increased risk of other sexually transmitted infections, e.g. HIV and HBV.

Transfusion transmitted serum hepatitis has been recognised since the 1940s, and was particularly common in recipients of blood products when large pools were used as the starting material. With no test for the infection, the measures taken to limit transmission were restricting plasma pools to 10 donations and removing donors from the panel when a patient developed hepatitis following a transfusion of their blood. Identification of an antigen shown to be associated with hepatitis (called the Australia antigen) was followed by approval of donation testing in July 1971. By December 1972 all donations in the UK were being tested for hepatitis B surface antigen (Gunson HH, 1996).

Accounts of AIDS in recipients of blood and blood products began to be reported in the literature in the early 1980s (MMWR, 1982; Amman AJ, 1983). With no test available, in September 1983 information was distributed to all donors, and potential donors, asking persons not to give blood if they thought they had the disease or were at risk of acquiring it (i.e. homosexual men with many partners, injecting drug users and sexual contacts of people with AIDS). A test for anti-HIV has been used for all donations since 14th October 1985. The criteria for excluding individuals with an increased risk of infection have been revised as more has been learnt about the epidemiology of HIV infection in the UK. As argued by others (Hewitt PE, 1994), and as shown later in this thesis, donor selection remains important as a means of reducing the number of anti-HIV positive donations entering the testing process and of reducing the risk of donations collected following infection but before antibody can be detected (Hewitt PE, 1994).

Transfusion transmitted hepatitis continued, albeit at a much reduced frequency (Howell DR, 1995), after the introduction of donor screening for HBsAg. The majority of cases were due to an unknown agent, so called non-A, non-B hepatitis (NANBH). Some countries introduced surrogate tests for NANB hepatitis. These tests were assays for hepatitis B core antibody (anti-HBc) and tests for raised levels of liver enzymes (e.g. ALT).

In the late 1980s a virus, to be named HCV, was identified by cloning nucleic acid from plasma of a chimp with NANBH (Choo Q-L, 1989). A diagnostic assay was first produced in 1990. Specificity of the tests was

improved by early 1991 and testing of all blood donations commenced in the UK on 1st September 1991.

Over the years there has been a steady introduction of available measures to reduce risks that have been recognised. Table 1.1 shows the tests for markers of transfusion-transmissible infection that are currently performed on all blood donations in the UK. The introduction of each of these tests has led to a reduction in the number of transfusion-transmitted infections. During the first full year of anti-HIV (1986) and anti-HCV (1992) testing in England and Wales 38 and 807 positive donors were identified respectively - thus preventing the donations from these donors entering the blood supply. As time passes following the introduction of a marker test, and the population of repeat blood donors passes through the testing process, the overall rate of infectious donations identified decreases. The number of positive donations excluded from the blood supply in England and Wales by donation testing during 1997 is shown in Table 1.1. Many of these HBsAg, anti-HIV or anti-HCV positive donations are expected to infect recipients if transfused. As donations are now processed into several components, an infectious donation has the potential to expose several recipients to infection.

Table 1.1 Routine testing for markers of transfusion-transmissible infection in England & Wales and the effect of testing on the prevention of infections in blood transfusion recipients.

Assay	Date of introduction to routine donation testing	Number of positive donations excluded by testing during 1997	Reduction in transfusion-transmitted infections in England & Wales following introduction of routine test*
Treponemal antibodies	by 1950	100 (1 in 21,703 donations)	Uncertain: it is difficult to ascribe reduction in transfusion-transmitted syphilis to testing since storage at 4°C leads to inactivation of *T.pallidum*.
HBsAg	early 1970's	123 (1 in 21,710 donations)	There was a marked fall in post-transfusion acute HBV infections. E.g. North London blood centre recorded 30 reports of cases in 1970, 12 in 1972, 6 in 1974 and 3 in 1976 (Barbara JAJ, 1981).
Anti-HIV 1 Anti-HIV 1&2	October 1985 June 1990	29 (1 in 92,079 donations)	There have been 69 HIV infections diagnosed that were probably transmitted by transfusion in the UK prior to 10/85#, and 3 that were transfused between 10/85 and the end of 1997.
Anti-HCV	September 1991	236 (1 in 11,315 donations)	Transfusion prior to 9/91 has been associated with 128 (4.3%) of laboratory reports of HCV infection with risk factor information (1992-1996) (Ramsay ME, 1998). Between 1/10/95 and 30/9/99 2 cases of HCV transmission by transfusion post 9/91 have been reported+.

* Other factors, such as improved donor selection, will have contributed.

Source: PHLS AIDS Centre (data as of 1st September 1998).

+ Source: SHOT Report, 98-99.

Maximising the effectiveness of donation testing includes assuring good test performance. Strategies to achieve this include the evaluation of test kits, and test kit batches, for suitability and reliability in the blood centre setting, before their use by transfusion services. Monitoring performance once a test is in use is also important.

Testing blood donations improves the safety of the blood supply in two direct, and quantifiable, ways:

1. Infectious donations found to be positive for markers of infection at the time of donation are removed.
2. Infected donors are excluded from the donor population, and infected donations are therefore prevented from entering blood centres in the future. In practice this is only assured if infected donors do not conceal information about their previous donation, and the blood service's information system identifies them as infected donors if they attend to donate again. On rare occasions infected donors may re-attend for re-testing, either deliberately or in ignorance, and more than one infected donation from the same donor may enter the testing system.

Testing also improves the safety of the blood supply in three indirect ways – more difficult to quantify and to distinguish the effects of each from each other and from other causes:

1. Donors who are at increased risk of blood-borne infections are excluded from the donor population. As blood-borne infections often have common routes of transmission, donors with evidence of one infection may be at increased risk of having other blood-borne infections that are not detected by donation testing.
2. Also, some individuals who have been in contact with infected donors (e.g. sexual contacts) may be at increased risk of infection and infected donations may be prevented from entering blood centres if these individuals are instructed not to donate blood.
3. The diagnosis of infection in a donor, and the surveillance of infections and risk factors in donors can improve methods of donor selection, for example, the detection of HCV antibodies in blood donors revealed a large group of donors who had been exposed to blood-borne infections by injecting drugs (MacLennan S, 1994): donor selection has been revised in the light of this finding.

Additional serological tests are performed in some countries. Some aim to detect infections missed by current testing, for example, HIV p24 antigen and

anti-HBc. Others detect transfusion-transmissible infections that are currently not tested for in the UK, for example, anti-HTLV. Others detect surrogate markers of infection, for example, ALT for hepatitis viruses, low pH hemagglutination for parvovirus B19, alpha-neopterin for detecting inflammation. The countries in which additional tests have been adopted have tended to have higher frequency of infections, and therefore of risk of transmissible infection, than in England and Wales. However, this is not always the case. Factors such as the expected risk of disease occurring in recipients, the amount of public concern about blood safety and the infection in question, and the availability of resources have also played a part in determining the differences in blood testing strategies in different countries. The availability of tests for nucleic acids provides an opportunity to detect infections that cannot be detected by serological tests. Donations collected during the window period of early infection are the main candidates. Nucleic acid testing (NAT) should detect infectious donations from seronegative donors and from any seropositive donors that routine serological testing fails to detect. Nucleic acid tests for HCV RNA were introduced during 1999 in the UK (with increasing implementation as a pre-release test for fresh components over the following 2 years), with testing of mini-pools of (96) plasma samples followed by further testing of smaller pools and individual samples of positive mini-pools. Initially the primary motivation to introduce this testing was compliance with requirements for manufacture of pooled plasma products (Flanagan P, 1998) but implementation was not halted when the UK stopped using UK sourced plasma for product manufacture. The potential additional benefit for a blood service of such procedures for specific agents will depend on the epidemiology of the agent in their population (see Chapter 5).

Assessing the value of additional donation testing strategies must consider some or all of the following costs:

- The cost of test kits and reagents and related laboratory costs including staff time
- The costs of confirmatory testing on reactive donations
- The costs of notifying, counselling, and referring donors who are positive to new tests, or who have persistent false reactivity to the new tests used

- The costs of replacing donors excluded because of positivity (or false persistent reactivity) to the tests used
- The costs of any delay in the release of blood components while testing is performed
- The costs of added data management and added complexity to the blood release procedure
- The costs of look-backs - that is, of tracing and testing recipients who may have been exposed to infection by earlier donations from donors found to be positive.
- Costs of litigation due to transmissions
- Costs of lost confidence in transfusion (psychological costs) and in the political system responsible for transfusion.

Control of production and administration

Certain manufacturing processes and conditions can reduce the probability of transmitting an infection by blood transfusion. Strict control of cleanliness during component production limits the opportunities for bacterial contamination. Storage of whole blood and red cells at 4°C ± 2°C limits the growth of many bacteria that may be present in blood.

Developments to testing systems, and controls on those systems, that ensure the release only of components that are negative for markers of infection have been a crucial factor in the improvement of safety gained by donation testing. Automation of testing, along with inclusion of controlled steps in commercial tests, has enabled strict standardisation and close monitoring of the testing process. One example of an important addition to the testing processes is sample addition monitors that change colour (measurable on a spectrophotometer) when serum or plasma is added. Another is process control automation. Use of appropriate quality control samples, as well as the manufacturer's controls, and "go-no-go" samples, adds a further check on test performance. The computerisation of test results and of component release has helped to increase safety in the face of increasing numbers of donations and the increasing volume of data generated during the testing of each donation.

Practices beyond the transfusion centre also contribute to the prevention of transfusion-transmitted disease. Strategies to avoid transfusion as a treatment unless absolutely necessary, and to inactivate viruses by heat or solvent detergent treatments of products, prevent exposures. Strategies to provide prophylactic treatment to recipients can also play a useful role. For example, HBV immunisation is currently recommended for haemophiliacs, those receiving regular blood transfusions or blood products, or those carers responsible for the administration of such products (Salisbury & Begg, 1996).

Manufacturing processes that involve pooling donations or components, e.g. for treatment with solvent detergents, require careful consideration. Pooling (unless the infection is neutralised by antibodies also present in the pool) can lead to an infectious agent in one donation entering multiple products, and should be avoided for that reason. Pooling is particularly dangerous with regard to agents that are not excluded by current testing strategies, including agents that are as yet unknown.

Maintenance of cold storage until used at the bedside, and administration with sterile equipment is also important.

Consequences of transfusion-transmitted infections

Infected recipients do not necessarily develop disease, and estimating the effect of infections requires knowledge about the natural history of infections.

Transfusion-transmitted infections also bear a risk of onward transmission. The major risk factors for transmission of the persistent viral infections i.e. injecting drug use and sexual contact may be relatively rare amongst transfusion recipients because of their health and high average age. However, this is not always the case and other types of contact - especially those common in health care settings - pose a risk of secondary transmission.

1.2 Estimation of the risks of infectious donations entering the blood supply

Quantifying the risk of transfusion-transmission of infection can be attempted by several methods - each method having different limitations.

Existing surveillance systems monitor diagnosed transfusion-transmitted infections. Several factors common to transfusion-transmitted infections, and to

transfusion recipients, are likely to contribute to a lack of clinically apparent symptoms and therefore to under-diagnosis of infections. Other therapies may negate or modify symptoms. For example, many transfusion recipients are receiving antibiotic drugs and are therefore less likely to suffer observable consequences from bacterial infections. Transfusion recipients are sick or injured, and often elderly, and have high mortality from other causes. The recipients who receive relatively large numbers of transfusions, and are therefore at the highest risk of transfusion-transmitted infections, have the highest mortality rates. Long pre-symptomatic periods are common for persistent blood-borne virus infections and occurrence of disease is therefore far removed in the future. This period may be reduced when infected by a larger viral dose, at an older age, and in already ill or immunocompromised individuals, but this is not always known. Even so, transfusion in the past may be overlooked as a possible route of infection when diagnosis is delayed for a period.

For some infections (for example, HAV and B19), naturally acquired immunity may be quite high – especially in older age groups – meaning that transmission of infection may be considerably less frequent than infectious transfusions. Also, asymptomatic infection is more common amongst the younger age groups who have the lower levels of naturally acquired immunity; so infection transmissions may not result in any disease. Recognised and reported cases of transfusion-transmitted infections are likely to be those with the more apparent, and more severe, clinical consequences.

There are therefore many handicaps to the recognition of transfusion-transmitted infections and these lead to ascertainment biases and limitations in data based on reports of diagnoses. Actively following up transfused recipients and testing them for evidence of transfusion-transmitted infections can overcome these. In the UK, transfusion-transmission of infection with observed clinical consequences is rare - both in absolute terms and relative to incidents of infection transmission by other routes. The number of recipients that need to be followed up in order to obtain a precise estimate of transmission rates is therefore very large and such studies have become prohibitively expensive. Table 1.2 shows some examples, using the *rule of three* to estimate binomial confidence intervals, (Armitage, 1998) of the number of subjects needed in cohort studies to produce a 95% CI that excludes a given transmission rate in

studies that observe no cases (assuming no loss of power due to loss to follow-up or error in recipient tracing) i.e. the minimum size of cohorts needed to demonstrate that the true transmission rate is lower than the given rate.

Table 1.2. Sample size calculations for transmission studies.

Transmission rate (per number of units transfused)	Number needed in cohort for 95% CI on transmission rate of zero (i.e. when no transmissions observed) to exclude given rate.
1 in 10,000	30,000
1 in 100,000	300,000
1 in 3 million	9 million
1 in 10 million	30 million

A recent study of over 22,000 units issued in London and the South East found no transfusion-transmitted HIV, HBV, HCV or HTLV I&II infections (Regan FAM, 2000). Another approach is to estimate the number of infectious donations that current donation testing is not expected to detect. To attempt such estimation, information is needed about infection rates in the population donating blood, about the development and persistence of the markers that are tested for and about the tests, and testing system, used. The probability of a donation being collected during the window period when the tests used cannot detect evidence of infection depends upon the incidence of the infection and the length of the window period. The probability of symptoms that may prevent donation occurring during this period may also need to be considered. Incidence is usually calculated using observations of seroconversions in repeat donors or observations of acute infections in donors. The predictive value of a negative test result depends upon the prevalence of the marker and the sensitivity of the test. The probability of a marker positive donation being released into the blood supply due to a failure, or error, in the testing system also depends upon the prevalence of the marker and upon the probability of a failure or error.

Table 1.3 shows some key items of information required to calculate theoretical estimates of the risk of a donation infectious for a given organism entering the blood supply. The range of values in which each of the variables in Table 1.3 might lie depends on the sample used to estimate the variable, the biological variability involved, and the assumptions made in obtaining the working value.

Table 1.3 Key information for estimating the risk of donations infectious for known pathogens entering the blood supply despite donation testing.

Component of risk	Information needed and source of that information	
	Derived from donation testing	Other sources
i. Risk of seronegative infectious donation being collected during early infection	• Incidence of infection in donors	• Length of the infectious seronegative window period following infection
ii. Risk of seropositive donation entering the blood supply through test failure or process error	• Prevalence of marker used to indicate infectivity in donations	• Sensitivity of tests for the marker • Rate of errors that could lead to failure to identify or withdraw a positive donation
iii. Risk of seronegative infectious donation being collected from donors with established (not early) infection		• Frequency of seronegative, infectious individuals (other than those in the window period following infection) amongst blood donors

Table 1.4. Published risk estimation studies.

Country , Year of data/ estimates (Reference)	Estimated risk of infectious donations per million donations (range[1])	Window period (WP) risk estimated	Length of infectious window period used in days (Range)	False negative (FN) & error risk estimated	Test sensitivity (S) & error rate (ER) used	Estimate for new donor donation included
USA, 1986-87 (Ward, 1988)	HIV 26	Yes	56 (28-98)	Yes No	S: 99% -	Partially WP=No FN=Yes
USA, 1987 (Cumming, 1989)	HIV 6.5 (3.33-11.33)	Yes	56	No Yes	- ER: 0.1%	Yes
USA, 1987 (Brookmeyer, 1994)	HIV 4.64	Yes	56	No No	- -	Yes
UK, 1986-87 (Hickman, 1988)	HIV: 1986 3.2 HIV: 1987 1.1	Yes	56	Yes No	S: 98% -	Partially WP=No FN=Yes
Australia, 1985-90 (Dax, 1992)	HIV: 1.08	Yes	28-42	Yes No	S: 99.69%	Yes
USA, 1991-93 (Schreiber, 1996)	HIV: 2.03 (0.36-4.95) HTLV: 1.56 (0.50-3.90) HCV: 9.70 (3.47-36.11) HBsAg: 6.65 (2.87-13.43) HBV: 15.83 (6.82-31.97)	Yes	22 (6-38) 51 (36-72) 82 (54-192) 59 (37-87)	No No	- -	No
USA, 1992-93 (Lackritz, 1995)	HIV: 1.52-2.22	Yes	Average of 25	No Yes	- ER: 0.5%	Yes
France, 1992-94 (Courouce, 1996)	HIV: 1.75 (0.3-4.6) HTLV: 0.17 (0.0-1.6) HCV: 4.48 (1.7-10.0) HBsAg: 3.13 (0.9-11.2) HBV: 8.45 (2.8-25.2)	Yes	22 (6-38) 56 (24-128) 66 (38-94) 51 (36-72)	No No	- -	No
Germany & Austria, 1993 (Schwartz, 1995)	HIV (Austria): 1.9 (0.7-4.8) HIV (Germany): 1.1 (0.4-2.6)	Yes	22	Yes Yes	S: 99% ER: 0.1%	Yes
Austria & Germany, 1994-5 (Riggert, 1996)	HCV (Austria): 111 (61-161) HCV (Germany): 208 (25-756)	Yes	74	Yes Yes	S: 98% ER: 0.1%	Yes
Australia, 1994-95 (Whyte, 1997)	HIV: 0.79 (0.22-1.37) HCV: 4.27 (2.82-10.01) HBsAg: 2.71 (1.70-4.00) HBV: 6.45 (4.05-9.52)	Yes	22 (6-38) 82 (54-192) 59 (37-87)	No No	- -	No
South Africa (Sitas, 1994)	HIV: 22(11-39)	Yes	34-98	Yes Yes	S: 99.9% ER: 0.1%	Yes
Germany, 1996 (Gluck, 1998)	HIV: 0.53(0.21-1.39) HCV: 8.8(3.3-31) HBV: 4.3(1.6-7.5)	Yes	22 82 56	No No	- -	No
Germany, 1990-95 (Koerner, 1998)	HCV: 1995 5(0.7-10) repeat HCV: 1995 50(36-67) new	Yes	74	Yes Yes	S: 98% ER: 0.1%	
EPFA countries[2], 1997 (Muller-Breitkreutz, 1999)	HIV: 0.43(0.18-0.82) HCV: 1.61(0.93-2.29) HBV: 2.51(1.57-3.70)	Yes	HIV: 22(6-38) HCV: 66(38-94) HBV: 59(37-87)	No No	- -	No
Thailand, 1990-93 (Kitayaporn, 1996)	HIV: 1990 380 (210-650) HIV: 1991 190 (100-340) HIV: 1992 200 (110-360) HIV: 1993 190 (50-670)	Yes	45	No No	- -	No
N.Thailand, 1989-94 (Sawanpanyalert, 1996)	HIV: 1,290 (880-1900) ·	Yes	45	No No	- -	No
Ivory Coast, 1991 (Savarit, 1992)	HIV: 5,400-10,600	Yes	56	Yes No	S: 99.0% -	Yes
Central & South America, 1993-94 (Schmunis, 1998)	HIV/HBV/HCV or T.cruzi: Average = 3,226	Different approach: estimates based on prevalence of infections and % of donations tested.				

[1] Various methods.

[2] Not-for profit blood services in Denmark, England, France, Finland, Germany, Scotland, Switzerland (NB data and estimates for Australia and American Red Cross are also included in paper).

Published estimates of the risk of viral transmission by transfusion for different blood services and different periods of time have varied in their methods and scope. Differences in the risk of infectious donations between the early days of HIV testing and more recent years (due largely to the reduced window period of more recent tests) and between countries of high infection prevalence and incidence and countries of low infection prevalence and incidence show clearly in the risk estimates produced for different years and countries. However, variations in the methods used to calculate risk estimates mean that relatively small differences in the estimates produced by countries using similar testing systems and with similar epidemiology are more difficult to interpret.

Table 1.4 summarises some published studies that have provided theoretical estimates of the risk of transfusion-transmitted infections. All of these studies have included estimation of the risk of window period donations (i.e. i. in Table 1.3) associated with donations from repeat donors. Some studies have included estimation of the risk of false negative results and errors (i.e. ii. in Table 1.3). In all, the risk of persistent (or fluctuating) seronegativity during established infections (i.e. iii. in Table 1.3) in blood donors has not been included or has been assumed to be zero.

In the USA the fall in the estimated risk of issuing HIV infectious donations between 1987 and the early 1990s was largely due to a reduction in the length of the window period used in the risk calculations (from 56 days to 22 days). The markedly higher estimated risk of HIV infectious donations in the Thai study is largely the result of the higher incidence of HIV infection in Thailand than in Europe and North America, although the longer window period used in this study also contributed to this higher estimated risk. The published studies have varied in whether they have estimated the risk from all donations, or just from donations from repeat donors. New (i.e. first time) donors differ from repeat donors in ways that affect the risk of an infectious donation entering the blood supply. Probably most important is that new donors have not been previously tested by the blood service for markers of infections used to exclude individuals from the donor panel. So, donations from new donors have a higher prevalence of infectious markers. Incidence of infection can be derived from donation testing in two ways; by testing donations for markers indicative of an early

infection (e.g. IgM class of antibody to hepatitis B core antigen, p24 HIV antigen, nucleic acids, or testing for low titre anti-HIV with recently proposed de-tuned antibody assays), or by using seroconversions in repeat donors that mark infections that have arisen since a previous donation. The former approach was not used in any of the studies listed in Table 1.4. All except one used the latter approach. Brookmeyer et al did not use donation testing data at all but utilised back-calculated estimates of the infection curve in the United States. Unfortunately seroconversions can only be observed in repeat donors: additional information and assumptions have to be used to obtain an estimate of incidence in new donors. Cumming *et al* used the prevalence observed in donations and assumptions about the time donors had been at risk of HIV infection to estimate incidence rates in donors tested for the first time. Lackritz *et al* used the prevalence observed in donations from new and from repeat donors during the first year of testing and assumptions about how the difference between these prevalences represented differences in incidence. Dax *et al* used the prevalence observed in donations and assumptions about the time course of HIV infection and about the probability of donating throughout that time.

More recently the use of de-tuned HIV antibody tests has been used to detect recent infections and to derive incidence (Jansen RS, 1998 and McFarland W, 1999). This method applies a sensitive and a less-sensitive (de-tuned) assay to samples and classifies samples that are positive to the sensitive assay and negative to the less-sensitive assay as early infections.

There has been no standard approach to the calculation of ranges around point estimates. Some studies have repeated the calculations using the "best" and "worst" values of some or all variables (e.g. window period length) to give the best and worst estimates. Some studies have used 95% confidence intervals around observed rates to allow for sampling variability in the data used.

One group has produced two studies that both used data from two countries (Germany and Austria) to produce comparable estimates for two blood services (Schwartz 1995, Riggert 1996). Another produced comparable estimates for a larger collection of blood services - those blood services collaborating in the European Plasma Fractionation Association's viral marker

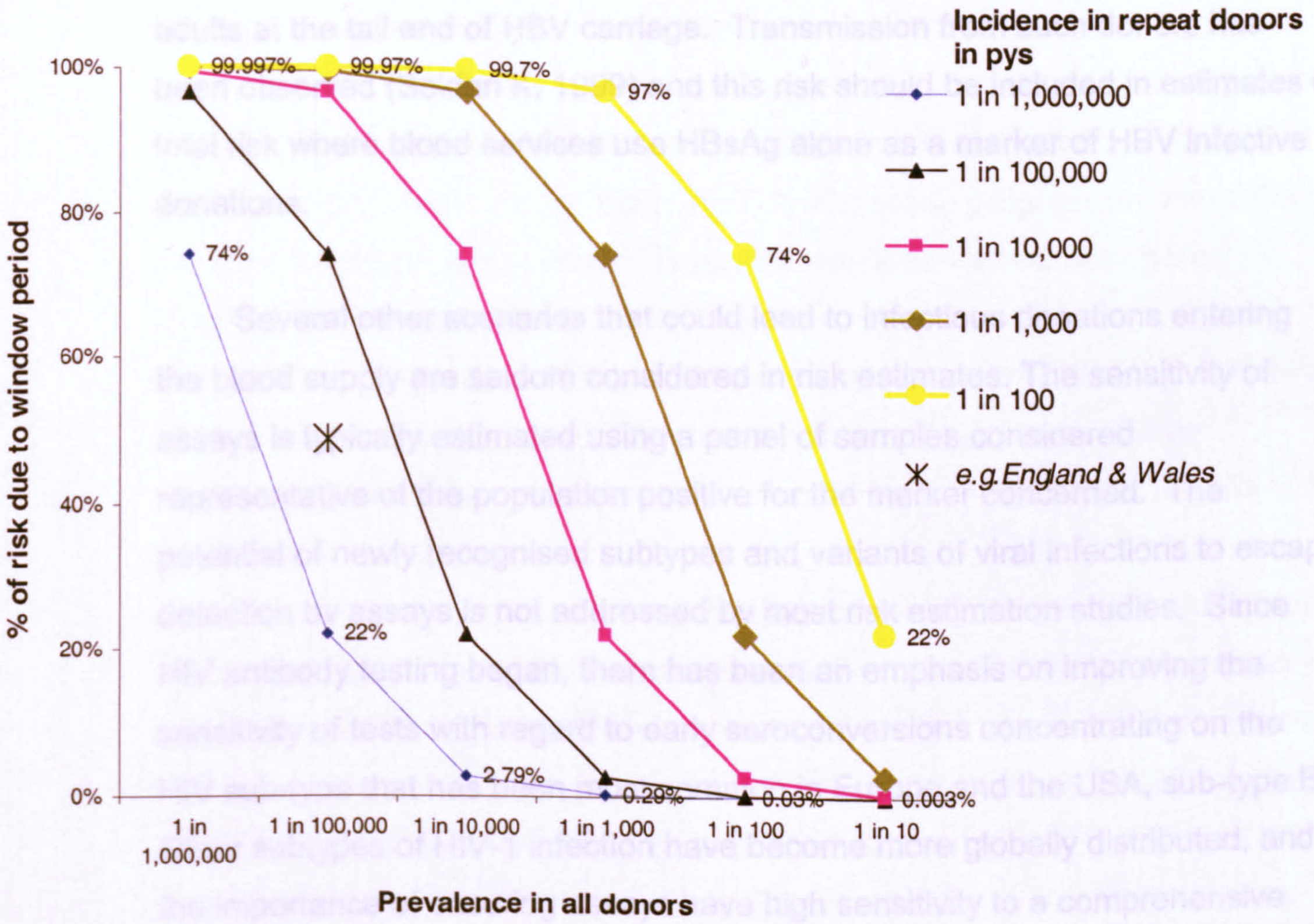
surveillance (Muller-Breitkruetz, 1999). The estimates for the 8 European collaborating blood services ranged from 0.05 infectious donations per million to 1.4 per million for HIV 1+2, from 0.43 to 4.97 per million for HCV and from 0.9 to 4.6 per million for HBV. As the same methods were used to generate the risk estimate for each blood service in this study, the differences in the risk estimates for the different blood services are - assuming the data submitted by each blood service were comparable - due only to statistical variability in the data used and to true differences in the risks dependent on the different epidemiology in the donors to the organisations.

Perhaps the most notable, and compelling, observation from reviewing these estimates is the disparity between the level of viral risk experienced in the less developed countries (e.g. Thailand, Ivory Coast) and that experienced in more developed countries (e.g. those in Western Europe and North America).

Studies frequently state that the risk of a donation being collected during the window period is the largest remaining risk of infection transmission (for infections that donations are tested for). This is often actually an assumption rather than a demonstrated fact. The relative importance of each component of the risk of accepting infectious donations varies between blood services depending on the specifications of donation testing, the proportion of donations collected from new donors and the rates of incidence and prevalence in the donating population. Figure 1.1 shows how the percentage of the total risk estimate due to the window period of early infection can vary with different prevalence and incidence. Many studies omit separate calculations for donations from new donors. However, donations from new donors consistently have higher prevalence and there are good reasons to expect they will also have higher incidence. The greater the proportion of donations collected from new donors the larger the contribution to the overall risk is that associated with donations from new donors (the Thai study reports that 76% of all donations were collected from new donors); and the greater the prevalence of infection the more important the risk of false negative tests and errors in the exclusion of seropositive donations. According to an analysis of data for England (Soldan K, Barbara J *et al* Unpublished work), 1993-1995, less than 10% of the total estimated risk of an HCV infectious donation entering the blood supply in England would be due to window period donations from repeat donors (if

window period for anti-HCV is 66 days (54-192), test sensitivity for anti-HCV is 98%, error rate is 0.5%). Studies that omit some components of risk or only consider donations from repeat donors would usually (to an extent dependent on their epidemiology and selection and testing practices) underestimate the risk of an infected donation entering the blood supply.

Figure 1.1 Variation in components of risk with varying prevalence and incidence



For an infection with a 22 day window period, using tests with 99.5% sensitivity and an error rate of 0.5%, e.g. HIV, and 11% donations from new donors.

In most risk estimation studies estimates of incidence based on seroconversions have been a key element. The use of seroconversions to estimate incidence involves an assumption that donors are not more likely to self-defer, either temporarily or permanently, after they have seroconverted and that the probability of an individual donating blood does not vary over the course

of antibody development after infection. There are some observations, such as longer than average inter-donation intervals in donors who have seroconverted for antibodies to HCV (Soldan K, 1998), and fewer than expected HIV p24 antigen positive, HIV antibody negative donations in the USA (Scheiber G, 1997), that suggest that donors are more likely to self-defer during the window phase. This may be due to a perception of recent risk, symptomatic primary infection, or perhaps just a disrupted life less conducive with donation around the time of their exposure to infection.

HBsAg negativity during established HBV infection can occur in healthy adults at the tail end of HBV carriage. Transmission from such donors has been observed (Soldan K, 1999) and this risk should be included in estimates of total risk where blood services use HBsAg alone as a marker of HBV infective donations.

Several other scenarios that could lead to infectious donations entering the blood supply are seldom considered in risk estimates. The sensitivity of assays is typically estimated using a panel of samples considered representative of the population positive for the marker concerned. The potential of newly recognised subtypes and variants of viral infections to escape detection by assays is not addressed by most risk estimation studies. Since HIV antibody testing began, there has been an emphasis on improving the sensitivity of tests with regard to early seroconversions concentrating on the HIV sub-type that has been most common in Europe and the USA, sub-type B. Other subtypes of HIV-1 infection have become more globally distributed, and the importance of ensuring assays have high sensitivity to a comprehensive range of HIV sub-types, should not be overlooked (Gurtler L, 1998). Mutant HBV infections, not detected by HBsAg tests, have also been shown to pose a risk (Jongerius JM, 1998).

Data that could verify or refute the results of risk estimation studies are rare. The introduction of nucleic acid technology (NAT) for testing donations should detect infectious donations missed by current serological tests and therefore provide some data to compare with the estimates. However, if the estimates from Europe and the USA are close to, or higher than, the true risk,

several years of data collection from NAT testing will be needed to test the accuracy of the estimates.

Use of risk estimate

The comparability of these estimates to other risks of morbidity is not straightforward. Infectious donations entering the blood supply do not directly translate to infected recipients and the actual risk of disease also depends upon the transmission rate, susceptibility of the recipient and the natural history of transfusion-transmitted infections in recipients. Information about natural history is often only available from case reports or from studies in other patient groups. The size of the infective dose, and the relatively poor health status of recipients, may make transmission, and rapid disease progression, more likely. On the other hand, some infectious agents may lose viability during their storage between collection and transfusion.

The communication and use of risk estimates is often difficult (Calman KC, 1997). Misunderstanding of these risk estimates, or ignorance of their limitations can lead to a false sense of confidence, or a false sense of alarm, in the safety of transfusion.

Only those components of risk that are known about are estimated and the accuracy of the estimates is only as good as the accuracy of the information used to derive them. While these estimates of the risk of infectious donations being accepted and entering the blood supply can be of value, they can give the misleading impression that the true and total infectious risk of transfusion is known. They should not be allowed to detract attention and resources away from un-estimated risks. The true infectious risks of blood transfusion involve both infections already known to be blood-borne (such as HBV, HIV and HCV), and those that have not yet been identified. The latter category may have considerable impact on blood services, for example the current concern and activity due to possibility of transmission of vCJD by transfusion (Barbara JAJ, 1998), and represents a potential hazard of transfusion that has been repeatedly realised as blood-borne infections have been recognised. These as yet unidentified risks justify the use of generic measures to limit the exposure of recipients such as restricting donation pooling, the use of viral inactivation and

the avoidance of unnecessary transfusion therapy irrespective of how low the estimated risks for HBV, HCV and HIV become.

1.3 Epidemiology of infections in blood donors and recipients: implications for public health

The testing of blood donations for markers of infectious disease has not only reduced the rate of transfusion transmitted infections, but has also provided opportunities for the relatively early treatment of the infections detected in "healthy" individuals (Seymour CA, 1994) and for the prevention of further transmission by other routes. Regional or national collation of the results of testing blood donations has contributed to knowledge about the frequency of infections in the population (McGarrigle C, 1997; MacLennan S, 1994). Comparisons of different geographical areas or different time periods can reflect differences in the frequency of infection in the population from which the donors come, or differences in the donor recruitment and selection, or donation testing, procedures. Despite the biases introduced by donor recruitment and selection, international comparisons (WHO, 1996; Naplas B, 1996) have typically provided rankings of infection rates that have concurred with information about infection rates in the population from other sources. The follow up of infected donors has also provided useful information about unrecognised, or unapparent routes of infection (Power JP, 1995; Hewitt PE, 1994). The collation of the probable routes of HIV infection of blood donors has contributed to the relatively scarce information about the extent of HIV transmission by sex between men and women in the UK (Gunson HH, 1991). The identification of newly acquired infections in repeat donors (i.e. the observation of seroconversions between donations) has been of particular interest as it has provided the opportunity to study the serology and infectivity of recent infections (Petersen LR, 1994), and to observe the complete natural history of infections that are typically only detected when clinical symptoms appear many years after infection. Information about seroconverting donors has also been used to identify and describe current, rather than past, probable routes of infection transmission (Soldan K, 1998).

In addition to the opportunistic use of data derived from donation testing and the follow up of donors found to be infected, the donor population has also

been used as a study base for special studies of the epidemiology and natural history of infections. The selection and recruitment of suitable controls for case-control studies is relatively easy and this study design has been used most recently to investigate risk factors for HCV infection (Goodrick MJ, 1994; Neal KR, 1994).

When considering the infectivity of blood from donors, and the natural history of infections transmitted by transfusion, knowledge obtained from observing infections transmitted by other routes may not be reliable. In particular, the progression of disease due to some viral infections may be affected by the infective dose. An infected blood component typically exposes a recipient to a far higher viral dose than other routes of transmission. Never-the-less, recipients exposed to infected blood have often been used for studying the natural history of blood-borne infections, particularly of the development of markers of infection and of symptoms in the early stages of infection, and of the onset of disease associated with chronic viral infections.

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Introduction

2.1 A brief history of blood transfusion

Records of transfusion of blood to human beings date back to one by Samuel Pepys over 300 years ago when Arthur Coga received a few ounces of sheep's blood before an audience with the Royal Society. James Blundell pioneered human transfusions during the 19th century, but it was the combination of the discovery of ABO blood groups by Landsteiner in 1900 and the impetus of the injuries of the two World wars and the Spanish Civil War that resulted in blood transfusion becoming an established medical therapy. History records the activities of several individuals as key to the development of blood transfusion therapy and of blood donors' organisations. Geoffrey Keyes became aware of the life-saving properties of blood transfusion whilst working as a medical officer during the First World War. He observed transfusion saving the lives of those who were in shock through loss of blood, and extending the possibilities of surgery. Returning to hospital work in London, Keyes was amazed at the lack of importance ascribed to transfusion and became an active promoter of transfusion among his colleagues. Resistance to consider the use of transfusion arose from the expense and awkwardness of direct transfusion as practised at that time. When his efforts to set up a donor panel at St Bartholomews were blocked he complained that "This prevailing uncertainty as

to how or where to obtain a blood donor often results in the postponement of the decision to transfuse until the patient has passed from the category of hopeful to hopeless" (said by Keyes, 1924). Meanwhile however, a layman was independently solving this problem. In 1921 a meeting of the Camberwell Division of the Red Cross was interrupted by a request for volunteers to give blood at nearby King's College Hospital. Percy Lane Oliver (1878-1944) was one of the members who went along to the hospital. Oliver's blood was not compatible with that of the patient but he was deeply impressed by the beneficial effect of the donation obtained from his fellow member - who rejoined them none the worse for her donation. So much so that he set about changing the situation he saw of patients who had neither relatives nor friends willing and able to donate blood being disadvantaged. Oliver put his public spirit and organisational skills to establishing a panel of volunteer donors to which hospitals had access strictly through his office. He arranged for hospitals that wished to use the service to blood group potential donors and he insisted on certain conditions and standards for the treatment of the donors at hospitals. His attention to the concerns and experience of the donors - whilst an annoyance to the hospitals - was crucial to maintaining the donor panel. For example, Oliver insisted on the use of sharp needles and the protection of donors from witnessing particularly distressing sights during the donating procedure (a common reason for donor resignation).

The Spanish Civil War provided impetus for, and experience in banking blood. Storage techniques had been proposed in the UK but had not been favoured over the use of fresh blood. After initial resistance it was again the imminence of war, in 1939, that prompted plans for four blood-storage depots in London funded by the Cabinet. The Medical Research Council (MRC) administered the depots on behalf of the Ministry of Health along with the Emergency Medical Service. The hospital based (Red Cross) panels became less in demand as the use of blood from the depots became standard. The Red Cross remained involved, along with other charities, in the organisation of panels and care of donors. In 1940 the need for depots outside London led to a scheme to establish a regional transfusion service. Depots bled in excess of

local needs in order to produce plasma. The service expanded and the processes developed and became more sophisticated throughout the war.

As the end of the Second World War approached it was recognised that although the depots were set up to meet the needs of air-raid casualties, the bulk of their work had actually been in connection with the civilian sick and it would now be impossible to return to hospital based donor services. The MRC, whilst maintaining a research interest, withdrew from taking on routine supply and organisation. In 1945 the Treasury accepted the solution that the Ministry of Health (MoH) should provide the National Blood Transfusion Service by continuing with the existing structure of 12 regional centres situated at Newcastle, Leeds, Sheffield, Cambridge, Oxford, Bristol, Cardiff, Birmingham, Liverpool and Manchester, and two centres, in Luton and Sutton, serving London and the South East. On 26 September 1946, the MoH took over full responsibility for transfusion services including training of staff and research into transfusion-related problems. The organisation of the service over the next 53 years has involved shifts of managerial responsibility (to regional health authorities and back to a centrally managed service), and changes in geographical location of blood centres (fully described by Gunson and Dodsworth, 1996). It has maintained a voluntary donor panel. Understanding of the clinical action of the components of blood and the separation of donations into those components has greatly increased the expertise involved in both the processing of blood donations and in the prescription of transfusions.

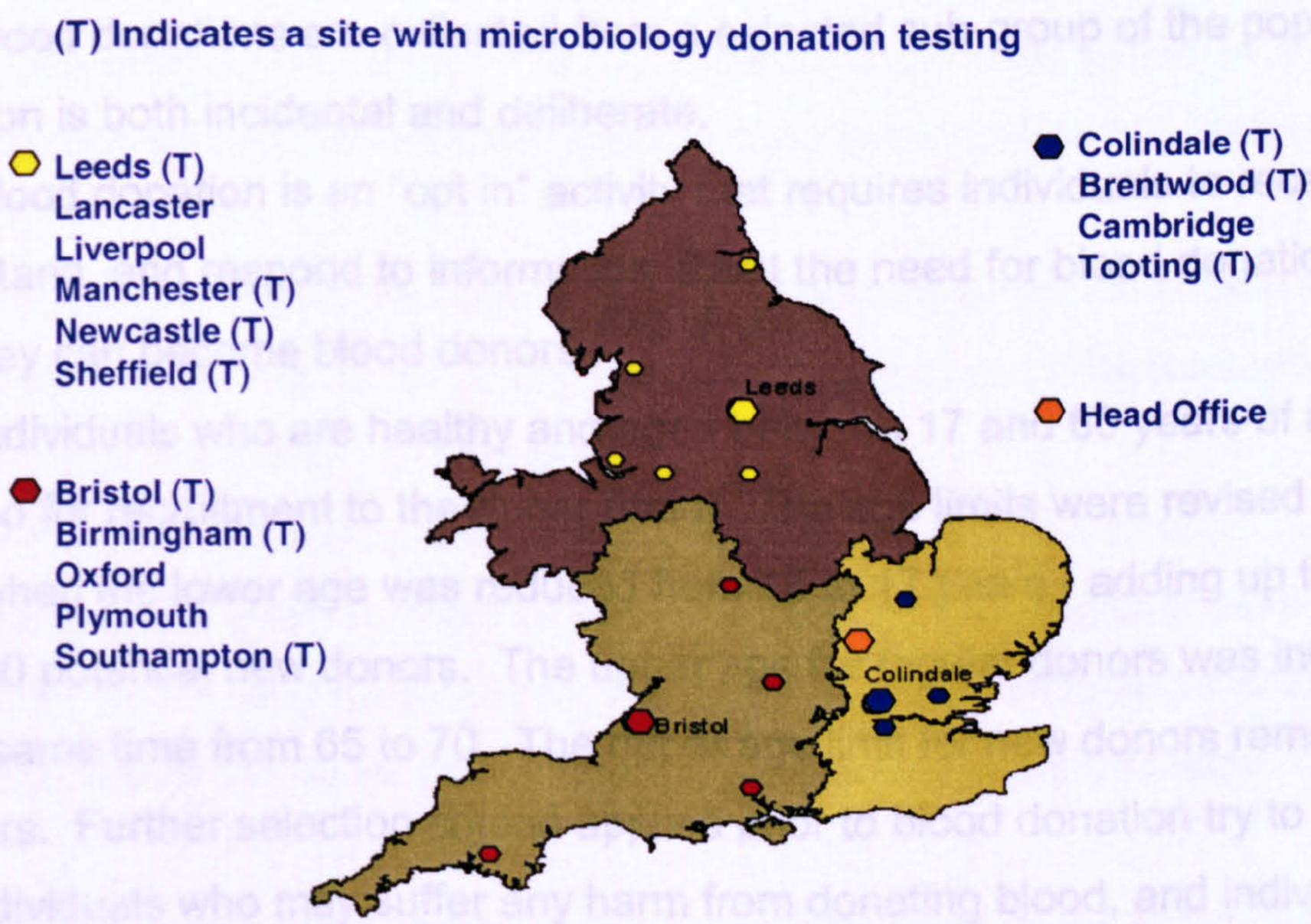
During the last 30 years, the transmission of infections by blood transfusion has had a great impact on the practice of transfusion medicine. One major consequence of the increased awareness of transfusion transmissible infections has been the development of microbiology and virology within the blood services to detect markers of infectious disease in donations. There has been an active relationship between transfusion microbiology and infectious disease epidemiology as knowledge gained by each has proved valuable to the other. The testing conducted on blood donations, and the observation of infections in recipients (when testing does not exclude infectious donations from the blood supply), has provided valuable sources of epidemiological information.

2.2 Current provision of blood transfusions in England and Wales

In 1993, the Department of Health in England established the National Blood Authority (NBA) as a Special Health Authority. Since that time it has taken on the responsibility for the management of the Bioproducts Laboratory, the International Blood Group Reference Laboratory and for the national co-ordination of the Regional Transfusion Centres (now called blood centres) - a task previously performed, to a lesser extent, by the now dissolved Central Blood Laboratories Authority and National Directorate of the National Blood Transfusion Service.

In July 1996, there were thirteen regional blood centres collecting, testing and storing blood in England, plus an Army blood supply depot. In July 1999, after reorganisation of the service, there were ten testing centres (see Figure 2.1). The Army Blood Supply Depot ceased collecting and testing blood from donors in July 1996. Blood centres remain in Cambridge (East Anglia), Liverpool (Mersey & North Wales) and Oxford but they no longer have full testing and processing capacity.

Figure 2.1 The Blood Centres of England



The Welsh Blood Transfusion Service (WBTS) is the responsibility of the Welsh Assembly and has one blood centre in Cardiff. The WBTS supplies plasma to BPL (when BPL are accepting UK sourced plasma) and functions similarly to the NBA on most operational matters. Donors in North Wales are recruited and managed by the blood centre at Liverpool (donations are tested by Manchester centre).

The English and Welsh blood transfusion services collect approximately 2.5 million donations each year. Donors can donate more than once each year and it can be estimated that 1.8 million donors are tested each year.

One component of the NBA's national co-ordination is donation testing and the collation of data arising from donation testing and from the investigation of post-transfusion infections.

The methods and processes of the blood transfusion services in the United Kingdom (England, Wales, Scotland and Northern Ireland) are standardised by the "Guidelines for the Blood Transfusion Service", more commonly known as "The Red Book" which is regularly revised by the Red Book Committee and its various specialist sub-groups.

Donor selection

Blood donations are collected from a selected sub-group of the population. Selection is both incidental and deliberate.

Blood donation is an "opt in" activity that requires individuals to receive, understand, and respond to information about the need for blood donations and how they can become blood donors.

Individuals who are healthy and aged between 17 and 60 years of age are targeted for recruitment to the donor panel. The age limits were revised in May 1998 when the lower age was reduced from 18 to 17 years - adding up to 600,000 potential new donors. The upper age for regular donors was increased at the same time from 65 to 70. The upper age limit for new donors remained at 60 years. Further selection criteria applied prior to blood donation try to ensure that individuals who may suffer any harm from donating blood, and individuals whose blood may cause harm to recipients are not accepted as blood donors. These criteria are collated in an appendix to the UKBTS/NIBSC Guidelines for

the Blood Transfusion Service as an A-Z of Guidelines for the Medical Assessment of Donors (as a controlled document).

Many of these selection criteria aim to lower the frequency of infectious diseases in the population who are accepted to donate blood. Individuals with any clinical signs or symptoms of a recent, or chronic, infection are not accepted. Individuals who have any behavioural, or lifestyle, characteristics that are associated with an increased risk of blood-borne infections are also not accepted.

Guidelines for donor selection also include some procedural instructions that may affect the effectiveness of the criteria themselves. All donors are asked to confirm that they have consented to their donations being tested for the presence of infections that might be passed on to patients, and told that they will be informed of the result. It is also emphasised to the donor that ill health within 14 days post-donation may indicate their donation would be unsuitable for use. In these circumstances they must inform the blood centre. Donation venues must have the following literature available:

1) Declaration to be signed by donors including the wording "I understand that I must read the literature explaining about HIV infection and AIDS. I agree that my blood donation can be tested for HIV (the virus associated with AIDS) and other infections that may be passed on by my blood. If my donation gives a positive result for any of these tests, I will be contacted for further tests and appropriate advice. I will inform the blood centre of ill health within 14 days post-donation as this may indicate that my donation would be unsuitable for use."

2) "Safety of Blood" leaflets. The most important exclusion criteria with respect to keeping the blood supply free from blood-borne infections are summarised on a leaflet. (Appendix 1).

3) Posters. Displaying information in 2).

Since 1999, every new donor has an individual interview that asks directly about their health, and their risks for infectious diseases including travel abroad, and a check that the donor has understood the Safety of Blood leaflet.

European legislation requires all blood donors to give informed consent to the procedure at each session. Since November 1998, a 'tick-box' health check

questionnaire has been printed on the back of the session slips (Appendix 2). All new donors and those who have not given blood for some time have a one to one interview with the session nurse or doctor, and all known donors complete the medical questionnaire while they are awaiting or when they register to donate at a session. This gives donors who are in high risk categories for infections the information and opportunity needed to exclude themselves before donating; it also gives the blood service documented evidence of donors' answers to the health questions.

The signature of the person completing the medical assessment must be recorded.

In addition to the routine medical assessment, apheresis donors have a full blood count and their serum albumin and total serum protein levels measured at the initial visit and then at least every 6th visit or annually, whichever is the shorter interval. A medical officer in the light of these results then assesses the donor's fitness for apheresis. Volunteers with a platelet count below 150 x 10^9/l should not undergo platelet apheresis.

Bacterial contamination can be introduced into the blood donation during the collection process. This risk can be reduced by techniques for cleansing the site on the donor's arm from which the donation is taken. The cleansing technique of all staff that carries out donation procedures is checked once a month (with swabs taken for bacteriology), to assess the effectiveness of arm cleansing in practice.

Component production and issue

Most blood collected from donors is processed into blood components and blood products. Blood components, such as red cell and platelet concentrates, fresh frozen plasma (FFP) and cryoprecipitate, are prepared from a single donation of blood by simple separation methods such as centrifugation and transfused without further processing. Complex processes, using the plasma from many donors as the starting material, are used to prepare blood products such as coagulation factor concentrates, albumin and immunoglobulin solutions.

This thesis is primarily concerned with blood components, and only concerns blood products to the extent that issues concerning donors overlap and because these two parallel uses of blood donations influence each other. Since May 1998 no UK-sourced plasma has been used for blood product manufacture in the UK. After a thorough cleansing and re-fitting scheme, plasma sourced from countries with no reported vCJD cases (the US) entered the product manufacture at the Bio Product Laboratory (BPL) in England and products derived from US plasma have been on release since November 1998. The epidemiology of infections in UK blood donors is therefore not relevant to blood products produced in the UK since 1998.

In most circumstances it is preferable to transfuse only the blood component or product required by the patient rather than using whole blood. This so-called 'component therapy' is the most effective way of using donor blood which is a scarce resource, and also reduces the risk of complications from transfusion of unnecessary components of the blood.

The average volume of whole blood collected is 450ml, taken into 63ml of anticoagulant. Up to three donations can be collected from a single donor during a year. Blood stored at 4°C has a 'shelf-life' of 5 weeks when at least 70% of the transfused red cells should survive normally. Alternatively, donors can give up to 15 litres of plasma per year by plasma apheresis: each donation providing 500-600ml of plasma. Platelets and leucocytes can also be collected by cytapheresis up to 24 times per year.

The processing of blood into components of varying constituents and varying therapeutic properties is an increasingly detailed subject. Only some aspects of component therapy are relevant to this thesis. Storage conditions of different components affect the risk of bacterial multiplication and the viability of some other agents. Red cells and whole blood are stored between 2 and 6°C for up to 35 days. Platelet concentrates (from the pooling of platelets 'recovered' from (usually four) whole blood donors and from apheresis from single donors) are stored at 20-24°C on a special agitator rack for up to 5 days. Fresh frozen plasma and cryoprecipitate is stored at -30° C for up to one year (and used within 4 hours of thawing). The cellular content of components affects the transmission of cell associated infectious agents. CMV, HTLV I&II,

and parvo B19 are associated with leucocytes and transmission of these viruses is less likely from acellular, or leucocyte depleted components

Donors who provide plasma and/or platelets and leucocytes by apheresis differ in their donation frequency and selection. Apheresis donors are selected from whole blood donors and have therefore already been through the donor selection and testing process at least once. The logistics of making apheresis donations requires the donor to commit more time to donating as well as to attend more frequently. Apheresis donation may therefore be inconvenient for individuals with a relatively busy job or life. While the additional donor selection probably acts to reduce the risk of blood borne infections the frequent donation pattern of apheresis donors means that should a donor acquire a new infection it is more likely that one or more donations will be collected during the infectious period.

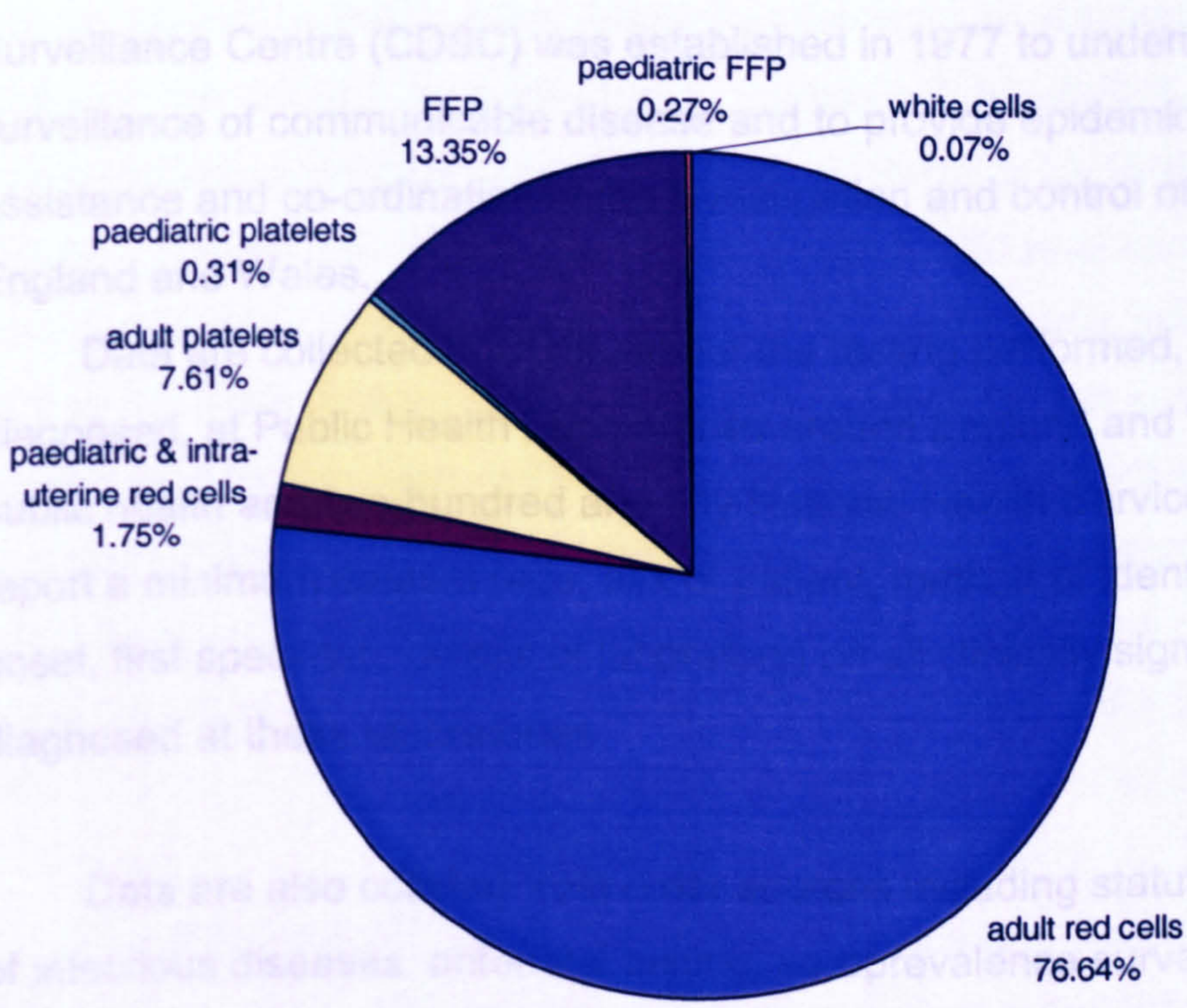
Certain components, for example platelets, are often prescribed for conditions associated with immunosuppression. Immunosuppression may make a recipient less likely to mount a detectable immune response, and more vulnerable to disease, if transfused with an infectious component.

Since a recommendation in July 1998 an additional stage of component production that may affect infection transmission has been introduced in the UK - routine leucodepletion. Prior to this recommendation 9% of red cell units and 23% of platelet components underwent leucodepletion of some kind. This action followed reports from the Government's Spongiform Encephalopathy Advisory Committee (SEAC), that there was a theoretical risk of the transmission by leucocytes of the infectious agent in variant Creutzfeldt-Jakob disease (vCJD). Monitoring of leucodepletion uses the guidelines produced by the Biomedical excellence and safety in transfusion group of the International Society of Blood Transfusion (ISBT) - with initial validation of the process followed by statistical process monitoring using a sample of components. Monitoring requires a standard of the reduction of the leucocyte count to less then $5x10^6$ leucocytes per unit transfused in at least 99% of components filtered with at least 95% confidence. By February 1999 all platelet products were being leucodepleted and progress towards supplying leucodepleted red cell components was ongoing. The process of leucodepletion may affect the transmission of infectious agents other than vCJD. Some cell-associated

viruses may be removed from components during leucodepletion. The effect of leucodepletion on bacterial contamination is uncertain: depending on the pre-filtration storage time and conditions, any bacteria contained in a blood donation may be ingested by leucocytes and so removed by leucodepletion or may remain free and unaffected by the phagocytic action of leucocytes.

During 1999, the English blood service provided over 2,893,627 components to 329 hospitals. These included 2,212,385 units of adult red cells, 50,383 units of paediatric red cells for newborn babies, 190 units of red cells for 'intra-uterine' transfusion, 219,556 adult doses of platelets, 8,887 units of paediatric platelets, 385,425 units of fresh frozen plasma, and 1,882 units of white cells (Figure 2.2) (NBA, 1999).

Figure 2.2 Components issued in England, 1999



Blood centres of England and Wales

The location of blood centres in England and Wales is shown in Figure 2.1. Donors registered with each centre live in the surrounding area, although donors may give blood elsewhere, for example, when on holiday. The donor's post-codes, and the site of the donation session (e.g. village hall, workplace, university campus) are linked to each donation record. Centres tend to predominantly supply their local hospitals, although blood components may be moved around the country to supply fluctuating demands.

Donors are recruited by advertisements in the press, on radio (usually designed and organised at local level), and occasionally by television advert campaigns (organised centrally). Existing donors are invited to encourage family and friends to consider becoming donors.

2.3 Surveillance of infectious diseases in England and Wales

The Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre (CDSC) was established in 1977 to undertake national surveillance of communicable disease and to provide epidemiological assistance and co-ordination in the investigation and control of infection in England and Wales.

Data are collected at CDSC about the testing performed, and infections diagnosed, at Public Health Laboratories around England and Wales. Forty-nine public health and two-hundred and fifty National Health Service laboratories report a minimum dataset (age, sex of patient, method of identification, date of onset, first specimen, details of laboratory) on all clinically significant infections diagnosed at these laboratories.

Data are also collated from other sources including statutory notifications of infectious diseases, antenatal testing, seroprevalence surveys and vaccine administrators. Other datasets that are used for investigating particular aspects of some infectious diseases include death registrations, hospital episodes and sentinel General Practitioner reporting.

Surveillance of viral hepatitis

Acute HBV infections confirmed by laboratories in England and Wales are reported to the PHLS CDSC. Laboratory confirmation of acute HBV infection includes a positive result of a test for HBV anti-core IgM (anti-HBc IgM), or a positive result of a test for HBV surface antigen (HBsAg) together with symptoms compatible with acute HBV and, if available, a negative result of a test for IgM antibodies to hepatitis A virus (HAV). Additional cases ascertained by contact tracing or other investigations, for example, during outbreaks or lookback at previous donations of a donor found to have HBV infection, are included in the surveillance if they have evidence of recent infection (anti-HBc IgM positive or seroconversion to anti-HBc IgG) even in the absence of clinical illness. Children infected by perinatal transmission and identified during the follow up of known high-risk mothers are also included. Surveillance reports include clinical and demographic details and information about risk exposure(s) in the previous 6 months. These details are based on information passed to laboratory staff by the clinician requesting the test and supplied with the results (Balogun MA, 1999). An audit of reporting has estimated 82% of laboratory confirmed acute HBV infections are reported (Ramsay M, 1998). Acute HBV infection may be asymptomatic or cause non-specific symptoms; about one-third of infections in adults are expected to be symptomatic and this surveillance cannot ascertain all acute HBV infections. Acute infection surveillance has been shown to give reasonable estimates of the incidence of symptomatic infection (Polakof S, 1984), and as the proportion of asymptomatic infections in adults is expected to be fairly constant over time surveillance of acute symptomatic cases can also be used to monitor trends in the incidence of acute HBV.

The PHLS CDSC has carried out surveillance of HCV in England and Wales since 1990. The aim of this surveillance is to monitor trends in incidence and prevalence, to determine the major risk factors associated with infection in England and Wales and to inform health care planning, prevention and control strategies (Ramsay ME, 1998). Surveillance information is derived from reports of confirmed HCV infections from laboratories in England and Wales. The low

proportion of acute HCV infections that are symptomatic (Locarnini S, 1996), the long but variable interval between acquisition and chronic disease (Alter H, 1996) and the lack of serological markers of acute infection (Clemens JM, 1992; Zaaijer HL, 1993) mean that these reports cannot be used to estimate current or past HCV incidence. Risk factor information is routinely reported from laboratories as part of the surveillance but the quality of this information is variable and the distribution of reported risk factors reflects the prevalence of testing in different risk groups. Some reporting laboratories have participated in enhanced surveillance involving the collection of more detailed clinical and epidemiological information about individuals with prevalent HCV infections and submission of serum for genotyping. Ad hoc surveys of testing and seroprevalence surveys have been used to further enhance the routine surveillance. Seroprevalence studies have involved archive samples from unlinked anonymous surveys of GUM clinic attenders, antenatal women and adults attending hospitals.

Further information about the epidemiology and natural history of viral hepatitis infections is obtained by surveillance of chronic liver disease due to viral hepatitis, notifications of acute clinical hepatitis, reports of deaths from viral hepatitis, hospital admission for viral hepatitis, surveillance of paediatric HCV, surveillance of occupational exposure to sources positive for blood borne viruses, surveillance of infections in prisons and a register of HCV infections with a known date of acquisition that can be followed-up for clinical outcomes.

Surveillance of HIV infection

Reports of newly identified HIV antibody positive individuals and AIDS cases are sent by microbiologists and clinicians to the PHLS CDSC AIDS & STD Centre. Reports include clinical and demographic details and information about risk exposure(s). Whenever possible enough information is gathered from the initial report or through subsequent follow-up to allow consistent allocation of individuals to defined risk categories. Where there has been exposure to HIV infection by more than one route, allocation to the most probable route for purposes of summary statistics is based on a hierarchy of

risk associated with different possible routes of infection. All reports indicating heterosexual exposure to HIV infection, but with insufficient information for further sub-classification by risk and country of exposure, and all cases reported as having acquired infection through heterosexual exposure in the UK with no evidence of "high risk" partners, are systematically followed up to clarify their exposure category (Evans BG, 1992).

Many HIV infections amongst groups of the population remain undiagnosed and therefore undetectable though surveillance systems based on routine laboratory and clinical diagnosis. To provide a more complete and accurate picture of the epidemiology of HIV infection in the community data from the HIV and AIDS reporting surveillance are augmented by several other sources of data. These include an annual survey of people currently receiving care for their HIV infection (Survey of Prevalent HIV infections Diagnosed - SOPHID (Molesworth AM, 1998)), behavioural surveys (Johnson AM, 1994), reports from genitourinary medicine clinics (Hughes G, 1998), mortality reports (Nylen G, 1999) and the surveys in the Unlinked Anonymous HIV Seroprevalence Monitoring Programme (DOH, 1999).

Surveillance of other infections

Reports of other confirmed infections - besides viral hepatitis and HIV infection - that can be transmitted by transfusion are also received at CDSC. Many of these come either on paper or electronically into the main database of laboratory reports - LABBASE. For example, CMV and parvo B19 infections are monitored. Microbiologists report a minimum dataset on all clinically significant infections based on information provided by the clinician requesting the test and receiving the result. The data reported includes age, sex of patient, method of identification, date of onset of illness, date of first specimen and details of reporting laboratory. Some risk factor information is reported for certain infections, but is very variable in quality.

Data collected by, or via, the NBA and the PHLS CDSC are the basis for the studies of the epidemiology of infection in blood donors and the assessment of the risk of transfusion transmitted infection included in this thesis.

2.4 Background to this study

Rational

The study of the distribution and determinants of infections in the donors of blood donations that are tested for markers of infectious diseases can inform transfusion practices and contribute to knowledge about infection in the general population.

Blood donation testing detects infections that are typically persistent but asymptomatic. As donors are selected to be individuals with no recognised increased risk of infection, unusual routes of infection transmission may be detected in this group. The serial testing of repeat donors enables the detection of incident infections. Some demographic information is available for the total population of donors tested and non-infected donors are available to provide more detailed comparative "control" information if needed.

Careful pre-donation selection of blood donors who are believed to be at low risk of blood borne infections, and the introduction of routine testing of all blood donations for markers of T. pallidum (1950), hepatitis B surface antigen (HBsAg) (1970), antibodies to the human immunodeficiency virus (anti-HIV) (1985, anti-HIV2 1990) and antibodies to hepatitis C virus (anti-HCV) (1991), has greatly decreased the risk of transfusion transmissible infections. However, the demand for transfusions is increasing and the infectious hazards of transfusing blood components continue to cause concern. As transfusion transmitted infections have become more rare the efficiency of prospective studies to determine actual transmission rates has been reduced and alternative methods of estimating transmission rates based on observed incidents in recipients and on infection rates in donors have become more important.

Additional interventions against transfusion-transmitted infections are available, for example, testing donations for HBV core antibody, HIV p24 antigen and human T cell leukaemia virus type I (HTLV-I) and use of virus-

inactivation procedures on components and the use of alternative therapies. Predicting the benefits of these proposed interventions, and evaluating their effect once introduced, requires accurate information about the risks and consequences of transfusion transmitted infections.

In order to assess the risks and consequences of transfusion-transmitted infections the characteristics of blood-borne infections, of donations, and of blood recipients need to be considered. Over the years, knowledge about new agents and about potential failures in the strategies to exclude known agents has increased. Consequently the range of possible strategies to exclude infections from the blood supply has also increased and debate about the risks of infection transmission by blood transfusion has become more complex.

Appreciation of the value of surveillance of infections in blood donors and recipients, along with falling infection rates, led to a proposal to establish enhanced surveillance of transfusion-transmissible infections. This was facilitated by changes in the blood service to make it more of a National organisation with standardised methods and services.

The study population

All blood centres in the British Isles and Republic of Ireland (except the five blood centres of the Scottish Blood Transfusion Service), opted to collaborate in an infection surveillance system, jointly run by the NBA and the PHLS-CDSC, by providing data about testing performed and about infections detected.

Clinicians and laboratories in England and Wales report blood borne infections - including those in blood transfusion recipients - to the PHLS-CDSC.

Aims

The overall aim of this work is to monitor and study the epidemiology of transfusion transmissible infections in England and Wales and to develop and apply methods for estimating the risk of infection transmission by transfusion in order to inform and evaluate donor selection and donation testing strategies,

and to contribute to knowledge of the epidemiology of blood-borne infections in England and Wales.

The following specific aims are addressed: -

1 Establish enhanced surveillance of transfusion transmissible infections

1.1 To develop methodologies for the national surveillance of infections in blood donors and of suspected and confirmed cases of transfusion transmitted infections in recipients of blood and non-fractionated blood components in England and Wales. This surveillance system will provide data that will be used for the following aims.

2 Descriptive epidemiology of infections in blood donors

2.1 To describe and monitor the prevalence and incidence of infections with HBV, HCV and HIV in blood donors and examine these data for evidence of temporal trends in the total sample and in sub-samples of donations from new donors, repeat donors and donors of specific sex and age groups.

2.2 To analyse the demographic characteristics (age, sex, ethnicity, region of donation) of blood donors infected with HBV, HCV and HIV.

2.3 To describe the probable routes of infection for HBV, HCV and HIV infected blood donors.

3 Descriptive epidemiology of post-transfusion infections in blood recipients

3.1 To describe the characteristics, frequency and outcome of post-transfusion infections diagnosed in blood recipients.

3.2 To identify any preventable factors contributing to the transmission of infections from donors to recipients in diagnosed post-transfusion infections.

4 To conduct related epidemiological studies using data from the surveillance system.

5 Calculation of estimates of the risk of transfusion transmitted infections

5.1 To use data from the surveillance system, together with data and assumptions from other sources to estimate the risk of transmission of HBV, HCV and HIV infection by transfusion.

5.2 To conduct sensitivity analyses of the data and parameters in the assumptions used to estimate risks.

5.3 To compare the estimated expected rate of transfusion transmitted infections with observed rates of transfusion-transmitted infections detected by the surveillance system.

Aims 1 to 3 are addressed in Chapter 3. Aims 4 and 5 are addressed in Chapters 4 and 5 respectively.

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3.1 Methods

3.1.1 Review of information available at blood centres

During the first half of 1995, each blood centre in England (14 centres) and Wales (1 centre) was visited (see Chapter 2: Blood centres of England and Wales). The methods of managing infected donors and post-transfusion infection cases, and the information about infections in donors and recipients that was available at blood centres were surveyed. This information was collected by the researcher (KS) during visits to each centre. Key members of staff including medical staff and laboratory staff were interviewed using a semi-structured questionnaire to ensure the same issues were covered at each centre.

Donation testing

The microbiology departments of the 15 blood centres were visited. Microbiology departments at blood centres used various automated and semi-automated systems for screening donations for markers of infection. Typically, microbiology departments had their own computerised systems for managing donation testing. These systems had often been locally developed, and had different specifications in different blood centres. Microbiology systems linked into the blood centres' mainframe computers to draw on information about donations for testing and to input information about donations to be withdrawn, and about donations to be released for issue. Microbiology computer systems did not routinely hold information about the sex, age or the donation status of donors: staff had access to the mainframe computer to obtain such details for donors who were found to be repeatedly reactive. Donations found to be repeatedly reactive by manufacturer's criteria were withdrawn and a sample referred for confirmatory testing according to algorithms agreed locally with the confirmatory laboratory.

Management of reactive donations varied between blood centres in the following ways: -

- Management of donors who were persistently repeatedly reactive to a test and had been repeatedly shown by confirmatory testing to be negative for the infection varied between centres, and within centres for different infections: in some cases, after two, or three, repeatedly reactive donations with negative confirmatory tests, donors were deferred from donation until such time as the test kit in use was changed, in other cases donors were repeatedly bled and their reactivity and confirmatory test results monitored, and in other cases, donations from donors who had been shown to be reactive to a specific test kit, but repeatedly negative to confirmatory tests, were tested by alternative test kits and, if negative to the alternative test kit, these donations were released into the blood supply.
- Repeat testing, and referral for confirmatory testing, of donations which were not reactive by manufacturer's criteria but which had abnormal results when compared to the bulk of non-reactive donations (i.e. donations

with results in the "grey zone") was standard at some blood centres, discretionary at others, and not done at others.

- Blood centres microbiology departments used various methods for managing information about donors whose donations had been repeatedly reactive to a screening test, including card indexes, log books and computer databases.

- Archive samples from positive donations were kept in various volumes (0.25, 0.5ml) for varying lengths of time (mostly 2 years).

Infected donors

Microbiology departments informed blood centre medical staff of donors with confirmed markers of infection. Medical staff responsible for the care of infected donors at the 15 blood centres were visited. Management of infected donors varied in the following ways: -

- Donors were informed of their positive test results by letter, by blood centre staff during a personal appointment (or occasionally a telephone conversation), or by their general practitioner (GP) depending on blood centre practice, the marker of infection and the geographical distance and travel restraints of the donor. (If seen again by the NBS, a blood sample was usually taken to re-confirm the infection.)

- If seen by blood centre staff, each blood centre performed discussion of histories of exposure to blood borne infection, and recording of this information, differently.

- If referred to GPs for follow up, some blood centres sought to obtain exposure history information (for some, or all infections) from the GP and some requested no further information after referral to GPs.

- Some blood centres periodically requested further information from the clinical centres managing their donors' long term care, and a few offered donors further testing over a number of years, and so obtained information about donors' disease progression.

- The infection status of each donor, including infected donors, was stored on blood centre mainframe donor computers (including range of 4 branded systems and several in-house systems). Further information about

infected donors was kept in paper files and sometimes also on computer databases.

- Blood centres did not consistently report donors with HBsAg to the PHLS-CDSC national surveillance. Reporting to PHLS CDSC and to local public health systems (Consultants in Communicable Disease Control (CsCDC)) was – at least in some cases – performed by the laboratory that performed the confirmatory testing; however it was uncertain how systematic and complete this reporting was.

Post-transfusion infections

Verbal or written reports about 15 blood centres' PTI investigation practices were obtained. News of cases of PTI reached the blood centres by various routes (e.g. hospital doctors, GPs, recipients, news reports, other blood centres). Information was usually directed to medical staff, but was occasionally received by Quality Assurance departments or microbiology laboratories and passed on to medical staff for management and investigation if necessary. Practices for investigating PTIs varied. One third (five) of blood centres did not have a standard operating procedure (SOP) for investigating PTIs in place. The practices detailed within SOPs and described by centres with no SOP in place varied in the following respects: -

- Criteria for initiating an investigation
- Information given to implicated donors and policies on recalling, or awaiting the next visit, of implicated donors
- The size of archived donation samples available and the use of these samples in testing implicated donors
- The extent of look-back at previous donations from an implicated donor

and

- The dissemination of findings (one centre reported its post-transfusion hepatitis infections to PHLS-CDSC national hepatitis surveillance, others left reporting to PHLS CDSC to reference laboratories (usually PHLs) performing the testing of samples. Again, the extent and nature of local communication about these infections with CsCDC was not clear or systematic.).

The following estimates and conclusions were made from the information obtained from blood centres about PTI investigations conducted between 1991 and early 1995:-

- approximately 50 investigations had been conducted each year
- three-quarters of these had involved HBV or HCV infections
- 1 in 5 of the post-transfusion hepatitis investigations had concluded that a transfusion was the probable source of the recipient's infection.
- Nearly half of the post-transfusion hepatitis investigations had been in the South and North West Thames Regions. How much this predominance was directly due to higher rates of post-transfusion hepatitis, and how much due to more frequent communication between hospitals and the blood centres about such cases was not clear.
- Other PTI cases investigated included infections with HAV, HIV, CMV, bacteria and parasites.
- While individual cases were well documented at most blood centres, potentially useful information about these PTIs had not been consistently reported to any national surveillance centre.

3.1.2 Review of current surveillance systems and data

Three surveillance systems for infections in blood donors were in place in 1994.

The surveillance system for HIV antibody testing of blood donations had been initiated when HIV antibody testing began in October 1985. All UK blood centres sent a monthly report form to a central collating centre (1985-1994 Manchester Blood Centre and from 1994 onwards The National Blood Authority). The form requested details about i) the test kits used during the previous month, ii) the total number of donations tested and the number of donations from new donors tested, iii) the number of donations (total and from new donors) which were initially reactive to the HIV antibody test, iv) the number of donations (total and from new donors) which were repeatedly reactive to the HIV antibody test, v) the number of donations (total and from new donors) which were referred for confirmatory testing and vi) the sex, vii)

date of birth, viii) number of previous donations and ix) the probable route of infection, if known, for each confirmed HIV infection detected. The form also asked for the results of testing of quality control specimens distributed by the Public Health Laboratory Service (PHLS).

In principle blood centres should also have been reporting all HIV positive donors to CDSC and their details entered into the national database of first confirmed HIV-1 antibody positive tests. In practice HIV positive donors were so rare that in most centres such reporting to CDSC had not become routine and reporting was not assumed to be complete. Each year, therefore, the NBS surveillance centre sent CDSC a list of the HIV positive donors identified so that centres could be prompted to complete reports for individuals not already reported to CDSC. Exposure history information was reported by blood centres to the NBS surveillance as free-text and was often unknown at the time of the surveillance report of the HIV infection: the probable route of infection was therefore often (90% of reports in 1994) not known by the NBS surveillance system.

A similar UK wide surveillance system for HCV antibody testing of blood donations had been initiated in September 1992 - one year after HCV antibody testing began in September 1991. Two forms were used for reporting HCV antibody testing information each month. One form requested numbers of donations tested, initially reactive, repeatedly reactive and sent for supplementary testing with a break down for donations from new donors and donations from previously reactive donors. A second form requested the RIBA and PCR results for donations receiving supplementary testing with a breakdown for donations from males and from females, and from new donors and from previously reactive donors. To allow time for supplementary testing to be completed, the second form was typically sent to the collation centre one month in arrears of the first form. No information about age or probable route of infection had been collected.

The data from both these NBS surveillance systems were collated and stored in DATAEASE databases. A set of standard summary tables was issued

each month to the reporting centres and to others with an interest in donation testing.

The completing of the surveillance forms was discussed in detail with the Head of Microbiology or the other staff member(s) designated to complete these forms at each blood centre. A number of variations in blood centre practices, in interpretation of the surveillance forms and in preparation of data for these forms were resulting in non-standardised information being collated by the surveillance centre.

For example, the eligibility of donations from previously reactive donors to be included in the monthly surveillance data about HIV and HCV testing had been understood differently by different centres, despite an attempt to separate these donations on the HCV antibody testing surveillance forms. Variation in the rates of reactivity to tests, as observed in the surveillance data, were therefore partially due to variation in the practices for managing, and for reporting, previously reactive donors.

In 1987 North London Blood Centre established a register of HBsAg positive donors (Howell D, 1991; Howell D, 1993). Centres were asked to make an initial report of all HBsAg positive donors previously identified, as far back as records would allow. Since that date, some centres had reported HBsAg positive donors as they were identified, and all centres had been asked annually to report each (unreported) HBsAg positive donor identified during the past year. Some data about donations dating back to 1972 were collected. The registry report requested donor identifiers, sex, date of birth, ethnicity or country of birth, history of any relevant exposures or symptoms and history of previous donation. For some years no reports had been received from some centres and some centres had not responded to each end of year check for cases not reported during the year. Absence of any reports from some centres, and quite marked fluctuations in the numbers of cases reported each year from other centres suggested underreporting to varying, unknown extents.

No national collation of the results of testing donations for Treponemal antibodies had occurred.

3.1.3 Establishing NBA/PHLS-CDSC joint surveillance system

i) Organisation and collaboration

A Steering Group was convened to advise and oversee the development of the surveillance system and of related studies of transfusion transmissible infections. Table 3.1 shows the members of this group and the time committed by each to the project. The group met at ad hoc times through out the study period.

Table 3.1 NBA/PHLS-CDSC steering group members

Steering group member	Time commitment to project
Scientist, PHLS-CDSC Immunisation Division	Full-time
Consultant Microbiologist, PHLS-CDSC Immunisation Division	Project supervisor: Involvement in ongoing work. (until October 1996)
Consultant Epidemiologist, PHLS-CDSC Immunisation Division	Steering group meetings (chair) & advice as requested up till October 1996. From October 1996 - Project supervisor.
Head of Microbiology, NBS-North London Centre, & Consultant in Microbiology to the NBA	Co-supervisor: Involvement in ongoing work.
Principal Scientist, PHLS-CDSC AIDS Centre	Periodic collaboration on HIV surveillance data. Steering group meetings & advice as requested.
National Quality Assurance Manager, NBA	Steering group meetings & advice as requested.
Director, Sexually transmitted and blood-borne virus laboratory	Steering group meetings & advice as requested.
Deputy Director, PHLS-Laboratory of Hospital Infection	Steering group meetings & advice as requested.

A group of blood centre and hospital specialists was convened during 1995 to develop a surveillance system for all serious hazards of transfusion (SHOT). The surveillance of PTIs developed in collaboration with this group so that it functioned in parallel with a system for surveillance of non-infectious complications of transfusion. (The scientist (KS) sat on the SHOT working group and the Consultant Epidemiologist (MR) sat on the SHOT Steering Group.) In order to improve the ascertainment and reporting of cases, the SHOT group took a number of steps to increase the awareness of the hazards (both infectious and non-infectious) of transfusion and to publicise the surveillance systems when the non-infectious complication reporting system was launched in November 1996. These included an editorial in the British Medical Journal, notices in various other journals and mailings to all hospital haematologists.

ii) Objectives and requirements

The objectives of the surveillance of infection in blood donors were: -

- To measure and monitor the initial and repeat reactivity rates to all test kit batches in use for testing blood donations at blood centres
- To measure and monitor the prevalence of markers for blood borne infections in first time (tested) blood donors
- To measure and monitor the incidence of markers for blood borne infections in repeat (tested) donors
- To describe the demographic (age, sex, ethnicity and geographical region) characteristics, clinical signs and histories of exposure to blood borne infections of infected blood donors

The requirements of the surveillance of infection in blood donors were: -

- A standardised surveillance system, covering all mandatory testing of blood donations, and all infected donors.
- Clear definitions of the information requested on surveillance forms.
- A format of data that would allow transfer of data electronically from blood centres to the collation centre when the IT system allowed.
- Staff at each centre trained to report, and responsible for co-ordinating reporting and for distributing results from the surveillance system within centres as appropriate

The objectives of the surveillance of infection in blood recipients were: -

- To monitor the number of post-transfusion infections which blood centres are informed about, and the probable source of these infections
- To collate and describe the failures of current blood centre practices to exclude HBV, HCV and HIV infections from the blood supply
- To collate and describe reasons for the occurrence of bacterial, parasitic and other viral (for which donations are not tested) infections in the blood supply
- To collate and describe the characteristics of transfusion transmitted infections in blood recipients

The requirements of the surveillance of infection in blood recipients were: -

- A standardised surveillance system, covering all post-transfusion infections in blood recipients about which blood centres are informed
- Clear definitions of the information requested on surveillance forms.
- Routine receipt of reports of suspected transfusion transmitted infections which are reported to PHLS-CDSC national infection surveillance systems
- Staff at each centre trained to report, and responsible for co-ordinating reporting and for distributing results from the surveillance system within their centres as appropriate

iii) Surveillance of infections: the system/general approach

In order to meet the objectives listed above, and with consideration of the availability of information at blood centres, a new surveillance system was developed.

The surveillance system was divided into three, linked systems- each collecting a different section of data: -

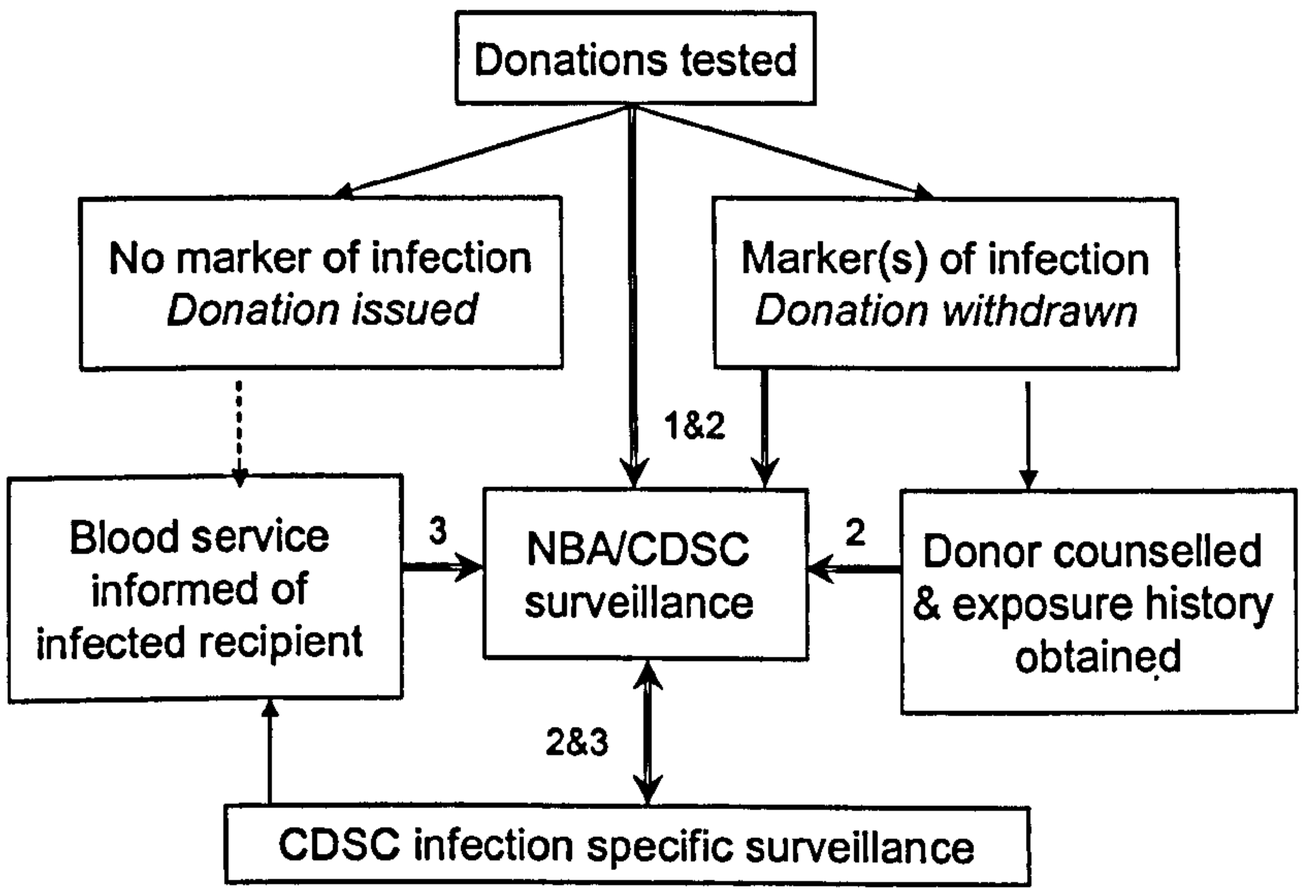
1. Data about donations tested, initial and repeat reactivity to test kit batches and confirmed markers of infection detected. (Donation testing surveillance - DTS)

2. Data about donors with a confirmed marker(s) of infection. (Infected donor surveillance - IDS)

3. Data about infections in transfusion recipients about which blood centres are informed, and investigations conducted into implicated donations. (Post-transfusion infection surveillance - PTIS)

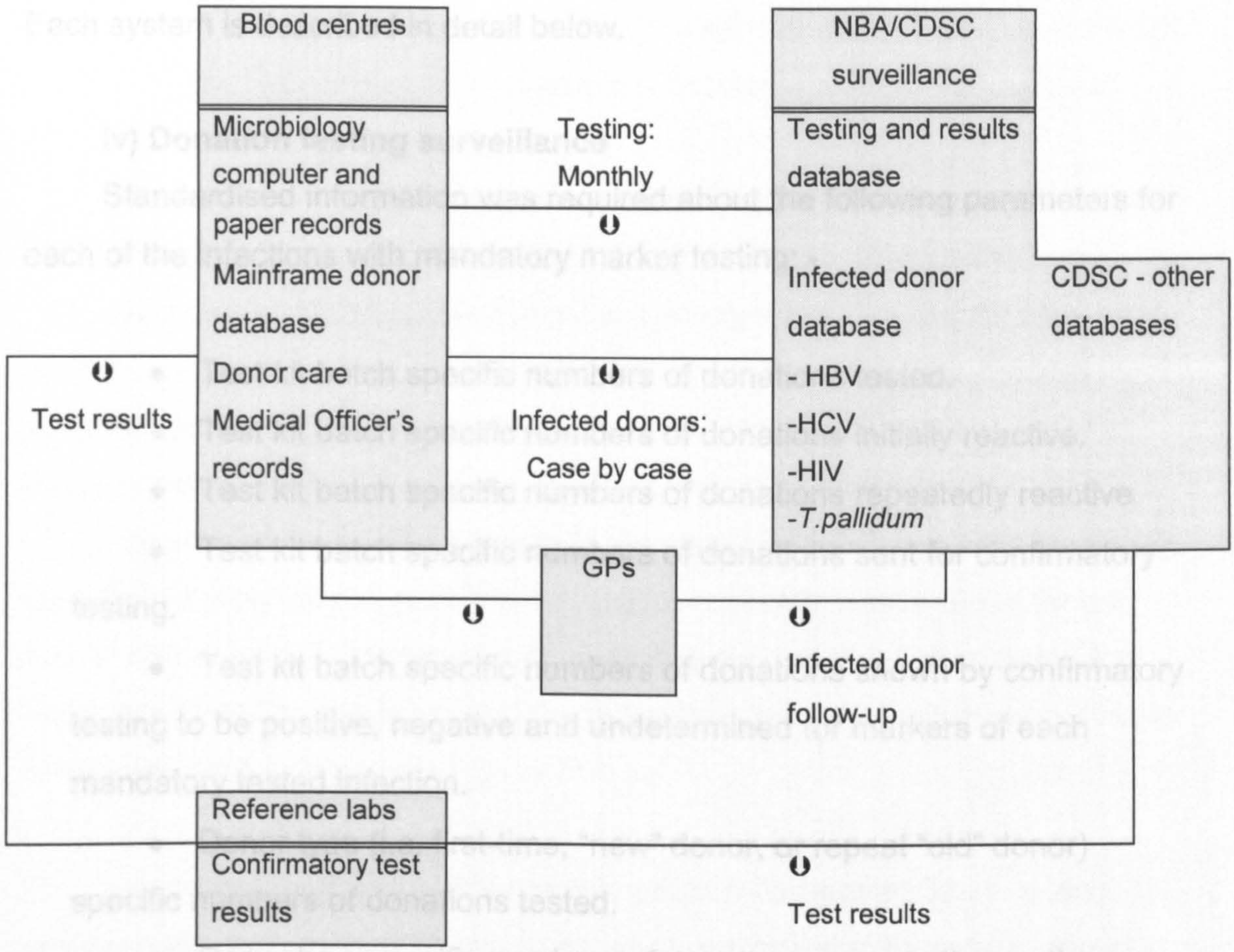
Figure 3.1 shows an overview of the NBA/PHLS-CDSC surveillance system. Figure 3.2 outlines the communications involved in generating the surveillance data relating to infections in blood donors.

Figure 3.1 NBA/PHLS-CDSC surveillance of transfusion transmissible infections



1. = Donation testing surveillance
2. = Infected donor surveillance
3. = Post-transfusion infection surveillance

Figure 3.2 Communication of information and surveillance reports



A set of surveillance forms was developed for each of the three surveillance systems. The format of these forms was determined by the data requirements and by the need for different pieces of information to be obtained from different staff within a blood centre, and at different times.

All the surveillance forms were printed on no-carbon-required double, or triple, A4 and A3 paper so a copy of each form sent to the surveillance centre could be kept at the blood centre. All surveillance forms were sent, in confidence, to the Medical Director of the National Blood Authority.

The three infection surveillance systems (DTS, IDS and PTIS) were introduced to blood centres in England, Wales, Northern Ireland, the Republic of Ireland, the Channel Islands and the Isle of Man on 1st October 1995. The Scottish Blood Transfusion Service (SNBTS) established a similar system for surveillance of donation testing in April 1995, and provided collated data, in a format comparable to the NBA/PHLS-CDSC surveillance data, to the

surveillance centre monthly. (The Serious Hazards of Transfusion (SHOT) surveillance system was introduced to UK hospitals on 1st November 1996.) Each system is described in detail below.

iv) Donation testing surveillance

Standardised information was required about the following parameters for each of the infections with mandatory marker testing: -

- Test kit batch specific numbers of donations tested.
- Test kit batch specific numbers of donations initially reactive.
- Test kit batch specific numbers of donations repeatedly reactive.
- Test kit batch specific numbers of donations sent for confirmatory testing.
- Test kit batch specific numbers of donations shown by confirmatory testing to be positive, negative and undetermined for markers of each mandatory tested infection.
- Donor type (i.e. first-time, "new" donor, or repeat "old" donor) specific numbers of donations tested.
- Donor type specific numbers of donations repeatedly reactive.
- Donor type specific numbers of donations sent for confirmatory testing.
- Donor type specific numbers of donations shown by confirmatory testing to be positive, negative and undetermined for markers of each infection for which testing is universal.

The donation testing surveillance monthly form pack (Appendix 3) consisted of six forms.

The first form (DTS Section 1) recorded the number of donations tested during the calendar month. The minimum requirement was the number of donations from new donors and the number of donations from repeat donors. Information about the number of donations tested by sex and by age group (<25 years, 25-34 years, 35-44 years and 45 years and over) was requested, but not required. The form asked for counts of donations from new donors to exclude, if possible, the following categories of donors:

i. Potential donors who attend a session, but do not provide a specimen for microbiological testing.

ii. Donors who have donated to other transfusion centres in the UK.

iii. Repeat donors who attend a session un-called/without their donor certificate.

iv. Lapsed donors i.e. donors who have not donated for a certain number of years or more (e.g. usually 2 or 5 - specified on the form).

However, as blood centre computer systems could not always promise to exclude such donors from the new donation count, the form also recorded whether each of the four categories may have been included in the reported data, so that a correction could be applied to the data if necessary.

The second form (DTS Section 2) recorded the number of initially reactive donations during the calendar month. One line of data was required for each test kit batch used during the month: test kit name, batch number, number of donations tested by the batch and the number of donations which were initially reactive to the batch.

The other four forms in this monthly pack (DTS Section 3 a, b, c, &d) recorded information (test kit batch, donation number, donation date, donation type, initial and repeat test results, and whether sent for confirmatory testing) about each donation tested (with a donation date within the calendar month) and found to be repeatedly reactive to the test used. In addition, the same information was recorded about all other donations sent for further testing in order to confirm a suspected infection. A separate form was used for each marker of infection (HBsAg, anti-HCV, anti-HIV and *T.pallidum* antibodies). The confirmatory laboratory conclusions were also recorded on these forms.

Screening results were defined as:

Initially reactive (IR) - a donation found to be reactive at or above the manufacturer's defined cut-off in the first test using whichever validated screening assay is used for donation release. These donations (unless within 6 months from a previously repeatedly reactive, confirmed negative,

donor being monitored) were withheld for repeat testing with the screening assay.

Repeatedly reactive (RR) - a donation found to be consistently (at least in duplicate) reactive at or above the manufacturer's defined cut-off in whichever validated screening assay is used for donation release. These donations (unless within 6 months from a previously repeatedly reactive, confirmed negative, donor being monitored) are sent to a reference laboratory for investigation.

Donation types for DTS Section 3 forms were defined as:

New - donations from donors who, according to blood centre records and donor self-report, have never been tested by a blood centre for this marker of infection i.e. from donors for whom available NBS records and self-reported information from the donor do not specify any donation to a UK blood centre before, and from donors who have not donated since the introduction of testing for the marker for which their test results are reported. This latter type of new donor in DTS Section 3 would be classified as a repeat donor in DTS Section 1. For such donations, blood centres were asked to label the record as ONT (old, not tested) on the DTS Section 3.

Previously reactive (PR) - donations from donors whose blood is not permitted to enter the blood supply because of one, or more, repeatedly reactive donation(s) within the last six months, or at the last, or last-but-one donation (i.e. so-called flagged donors or X-filed donors). In practice this may include donations from donors who were previously reactive to the current test or to another test for the marker used in the past.

Not previously reactive (NPR) - repeat donors whose blood is eligible (pending donation testing) for the blood supply. These donations are from donors, who have been tested for the infection marker before, but have either never been repeatedly reactive, or who have not been repeatedly reactive at the last, and last-but-one donation or during the last six months.

Confirmatory laboratory conclusions for DTS Section 3 were defined as:

Positive - found by the confirmatory laboratories tests and interpretation to be positive for the marker of infection.

Negative - found by the confirmatory laboratories tests and interpretation to be negative for the marker of infection.

Undetermined - found by the confirmatory laboratories tests and interpretation to be neither positive nor negative for the marker of infection, but concluded to be of undetermined marker status at this time.

Blood centres were asked to exclude the following samples from the reported data on each form:

i. Samples taken to re-confirm an infection in a donor i.e. "diagnostic" samples.

ii. Non-blood donor samples, e.g. antenatal samples, organ/tissue bank samples.

iii. Autologous donations i.e. donations collected from an individual for transfusion to the same individual at a later date.

and to also exclude from the Section 3 forms,

iv. Donation samples referred for antibody quantification for immunoglobulin preparation.

Donation testing surveillance forms were sent to the surveillance centre as soon after the end of each calendar month as possible, and by the 15th of the following month at the latest; complete confirmatory laboratory conclusions were not always available. Second copies of the DTS Section 3 forms, with completed confirmatory laboratory conclusions, were sent with the following months data if updated information was then available. If no report had been received by the surveillance centre for the last month, or if any confirmatory laboratory conclusions remained outstanding for the last but one month, the

blood centre was contacted by the surveillance centre and asked for the missing data.

Data were generally summarised and analysed as frequency of reactivity and positive donations per 100 and per 100,000 donations tested respectively.

During 1999, two routine analyses of the monthly donation testing data were developed -

Analysis of Monthly donation testing data

The aim of this analysis was to identify overall repeatedly reactive rates and infected donor rates for the most recent month that were outside the 95% prediction intervals based on the previous 36 months observed data (i.e. to alert to major changes in repeat reactivity and infection rates in blood donations collected by all reporting centres, possibly indicating a change in testing performance, donor selection or national infection rates in the donor population).

Programmes were written in GLIM (by Nick Andrews) to model the observed data (numbers tested, found repeatedly reactive and found confirmed positive) for the previous 36 months in order to predict an expected range, at a set level of confidence, for rates during the current month. Each month the data files were up-dated and the analyses re-run. The model gave out-lying observations during the thirty-six month period a lower weighting in the prediction of expected rates so that previous unusual observations did not make the model insensitive to changes in the observed data that might be of importance. The output gave the raw data for the month, the observed rates, the expected rates, the low and high limits of the ranges of expected rates (at a set confidence level) and a score of how much each observed rate differed from the expected rate. This score, called the exceedance score, reached 1 when the observed rate was equal to the high limit of the expected rate and -1 when the observed rate was equal to the low limit of the expected rate. Exceedance scores of less then -1 or greater than 1 where therefore flagged as "unusual" observations.

$$\text{Exceedance score} = \frac{(\text{observed rate} - \text{expected rate})}{(\text{high limit of expected rate} - \text{expected rate})}.$$

The model was run twice each month - once at the 95% confidence level and once at the 80% confidence level.

Analysis of centre distribution of infected donors

The aim of this analysis was to identify centre specific proportions of all infections, during the current year, that were outside the 95% probable range of expected values based on the previous 3 years' data (i.e. to alert to a relative change in infection rates at any one centre, possibly indicating a localised increase (or decrease) in infections in the donor population). The smaller testing centres were excluded: data from 14 centres in British Isles entered this analysis each month.

Chi-squared analyses were performed by EXCEL to compare the distribution of infections between centres during the most recent six months with the distribution of infections between centres during the previous twelve months. Each month the "data" spreadsheet was refreshed with an update from the donation testing database and the outputs on the "results" spreadsheet were automatically re-calculated.

Chi-squared values indicating an observed rate for any centre outside the 95% confidence interval on the rate observed during the previous 3 years were flagged as "unusual" observations. Unusual observations were summarised each month in a table showing the number of consecutive months for which this result had been flagged as unusual.

v) Infected donor surveillance

The infected donor surveillance form pack (Appendix 4) consisted of two forms.

The first form (IDS Section 1) recorded demographic (sex, date of birth, post-code) and previous donation details (when, where and test results for the most recent previous donation) about the donor of each donation with a confirmed marker of infection (HBsAg, anti-HCV, anti-HIV or *Treponemal* antibodies) and the details of all confirmatory tests performed on the donation. This form was designed for completion from blood centre records when the confirmatory laboratory conclusion was received.

In order to match the infected donor surveillance reports to donation testing surveillance reports of donations with confirmed markers of infection, the donation number was required on both the DTS and the IDS surveillance forms. In order to identify each infected donor, and to match infected donor surveillance reports to surveillance reports from other sources to the PHLS-CDSC, the soundex code of each donor's surname, and their first initial and date of birth were also required on the IDS forms. (Soundex codes are not unique for a single surname. Mainly because soundex codes ignore vowels, all soundex codes can relate to several names, for example, H300 is the code for Hutt, Heite, Hyde and Hoade, among many possibilities. However, if the soundex code is used in combination with the first initial, date of birth and sex, matching reports, and duplicate reports, can be identified and reports for an individual can be updated if additional information becomes available.) The extent of erroneous matching due to identical soundex and date of birth for different individuals has not been estimated. The probability of an infected donor record with identical soundex and date of birth and within the same region and the same period of diagnosis as another infection record is expected to be very small and erroneous matching is unlikely to cause error in the information collected. Instructions for the manual coding of surnames into soundex codes and a programme for the computer generation of soundex codes were sent to blood centres when the revised surveillance system was introduced.

The second form (IDS Section 2) recorded the donor details that only became available when a blood centre clinician, or other carer, subsequently communicated with the donor about the infection that had been detected. These details were: the donor's history of exposure to blood borne infections, the ethnic group of the donor (ethnic group is sometimes available from blood centre records, and reported on IDS Section 1), the donor's country of birth and whether the donor had any clinical signs of the infection. Ethnic group information was requested to be based on donor self-report i.e. asked as "To which ethnic group does the donor consider himself/herself to belong?" The first version of this form also recorded how this information was obtained: from

personal interview, from blood centre records, or from some other source e.g. GP or clinician to whom donor referred for further care.

If a IDS Section 1 was not received at the surveillance centre for a donation reported as positive by the DTS Section 3, a reminder was sent to the blood centre, initially during the quarter following the donation date and again each quarter as necessary (changing to by six-month periods from Jan 1997). Besides increasing reporting, this also functioned as a check that all positive donations reported to the donation testing surveillance were unique positive blood donors (i.e. resulted in detection of duplicate test reports for the same individual, or reports of samples other than blood donations). If an IDS Section 2 was not received, a periodic reminder was also sent, until the surveillance centre was informed that follow up of this donor had been closed without IDS Section 2 information being made available.

Follow-up of selected Infected Donor reports was conducted during the study period for various purposes e.g. to identify seroconverters, to investigate sources of infection that were unusual or possibly of public health interest e.g. infections reported to have been acquired in hospitals or in schools.

vi) Post-transfusion infection surveillance

The post transfusion infection surveillance pack (Appendix 5) initially consisted of three forms.

These forms were for reporting to the surveillance centre all infections (including HAV, HBV, HCV, HIV, bacterial and parasitic infections) in transfusion recipients about which blood centres were informed, and to subsequently report a summary of any investigations of the implicated components.

Information about the recipient, the recipient's infection and the transfusion(s) implicated as the possible source of infection formed the basis of the initial report. Subsequently, after appropriate investigations had been completed, details about the findings of the investigation were reported on the other two forms.

The first form (PTIS Section 1) recorded each post-transfusion infection which blood centres were informed about. A post-transfusion infection (PTI) was defined by the following criteria:

- The receipt of transfusion had been confirmed.

and

- Infection in the recipient had been confirmed (by detection of antibody, antigen, RNA/DNA, or culture of an organism).

and

- There was no evidence that the recipient was infected prior to the transfusion.

or,

- The receipt of transfusion had been confirmed.

and

- The recipient had had a diagnosis of acute clinical hepatitis of no known cause (i.e. including no evidence of acute HAV, HBV, HCV, EBV, or CMV infection in post-transfusion samples to date).

This second definition was necessary to include cases of post-transfusion hepatitis of unknown type, and cases of post-transfusion HCV where serological markers of infection were not yet detectable.

One category of post-transfusion infections was exempt from reporting. The exception was for HCV or HIV infected recipients whose implicated transfusion(s) were not tested for anti-HCV or anti-HIV (i.e. transfusion under investigation occurred prior to the introduction of testing). These cases were exempt from reporting as they were frequent, often inconclusively investigated, and not informative about current blood safety.

If other possible sources of infection were known for a post-transfusion infection, an initial report was still requested.

This form recorded details about the recipient (soundex code, first initial, sex, date of birth, significant test results on pre- and post-transfusion samples, infection, date of onset of symptoms, date of diagnosis and history of other risk

factors for infection) and about the transfusion (reason for transfusion, place of transfusion, date, type and number of components transfused). PTIS Section 1 also recorded whether, based on available information about the recipient and the implicated donations, an investigation of the implicated donations had been initiated.

The second (PTIS Section 2), and third (PTIS Section 3), forms recorded the outcome of any investigation of implicated components. PTIS Section 2 recorded the testing performed on samples from the implicated donations and donors. PTSI Section 3 recorded the conclusions of the PTI-case investigation. If one or more component(s) implicated in the PTI case had been produced by blood centre(s) other than the one which was informed of the PTI, copies of PTIS Sections 2 and 3 could be sent to the relevant blood centre(s) for completion and return to the case-initiating blood centre.

A probably transfusion-transmitted infection (TTI) was defined by the following general criteria: -

For viral infections: -

- Re-testing of the archived sample of an implicated donation found the donation to have markers of infectivity.

or

- Testing of subsequent samples obtained from the donor of an implicated donation found the donor to have markers of infection consistent with the donor having been infectious at the time of the implicated donation.

For bacteraemias: -

- Testing of the implicated donation found evidence of an organism also found in the recipient, or, in the absence of an organism identified in the recipient, of an organism expected to cause the symptoms observed in the recipient.

and

- No evidence that contamination of the implicated donation occurred after the transfusion was stopped.

Specific criteria applicable to the majority of cases are shown in table 3.2.

Table 3.2 Specific criteria for classification of post-transfusion infections as transfusion- transmitted infections.

Infection	*Donation archive*		*Donor*		*Recipient*[1]
HBV	HBsAg positive *or* HBV PCR positive	&	No tests performed after implicated donation, *or* Evidence of HBV infection at some time after implicated donation	&	Evidence of HBV infection (of same sub-type if known)
or,	No testing *or* Negative for all serology tests for HBV (with or without DNA)	&	Markers of acute HBV infection found <6 months after implicated donation, *or* Symptoms of acute hepatitis during 6 months after implicated donation and markers of HBV infection found subsequently, *or* Markers of resolved infection or HBV carriage found >6 months after implicated donation (without known date of infection after the implicated donation).	&	Evidence of HBV infection (of same sub-type if known)
or,	HBsAg negative, anti-HBc positive, anti-HBs negative/wk	&	No tests performed after implicated donation, *or* Same as archive, with or without a history of hepatitis.	&	Evidence of HBV infection (of same sub-type if known)
Infection	***Donation archive***		***Donor***		***Recipient***
HCV	Anti-HCV positive *or* HCV antigen positive *or* HCV PCR positive	&	No tests performed after implicated donation, *or* Evidence of HCV infection at some time after implicated donation.	&	Evidence of HCV infection (of same sub-type if known)
or,	No testing *or* Negative for all tests for HCV	&	Markers of HCV infection found after implicated donation (without known date of infection after the implicated donation) *or* Symptoms of acute hepatitis during 3 months after implicated donation and markers of HCV infection found subsequently.	&	Evidence of HCV infection (of same sub-type if known)
Infection	***Donation archive***		***Donor***		***Recipient***
HIV	Anti-HIV positive *or* HIV p24 Ag positive *or* HIV PCR positive	&	No tests performed after implicated donation, *or* Evidence of HIV infection at some time after implicated donation.	&	Evidence of HIV infection (of same sub-type if known)
or,	No testing *or* Negative for all tests for HIV	&	Markers of HIV infection found after implicated donation (without known date of infection after the implicated donation), *or* Symptoms of seroconversion illness during 3 months after implicated donation and markers of HIV infection found subsequently.	&	Evidence of HIV infection (of same sub-type if known)
Infection	***Donation archive /component***[2]		***Donor***		***Recipient***
Bacteria	Markers of specific bacterial infection *or* Cultures specific	&	No tests performed after implicated donation, *or* Evidence of specific blood borne bacteria, or of specific bacteria colonising venepuncture site, at some time after implicated donation.	&	Evidence of specific bacterial infection of same species and type as far as known, *or* Symptoms typical of specific bacterial

	bacteria				infection.
or,	No testing *or* Negative for all tests for bacteria	&	Evidence of specific blood borne bacteria, or of specific bacteria colonising venepuncture site, at or after time of implicated donation. or Symptoms of specific bacterial illness during month before or after implicated donation and any permanent markers of specific bacterial infection found subsequently.	&	Evidence of specific bacterial infection of same species and type as far as known, *and* no other identified source of infection.

Infection	***Donation archive/ component***		***Donor***		***Recipient***
HAV	No testing *or* anti-HAV positive	&	Acute HAV infection diagnosed during post-transfusion period	&	anti-HAV positive
or,	as above	&	anti-HAV positive	&	Acute HAV infection post-transfusion
Malaria	No testing *or* positive for plasmodium or malarial antibodies	&	Positive for malarial antibodies	&	Malaria diagnosed within x weeks of transfusion.

1. All without other proven source of infection, and without evidence of infection prior to transfusion, and with disease (or markers of infection) within limits of possible incubation periods.

2. If index component used then absence of evidence of contamination having occurred after the transfusion is also required.

All cases meeting these criteria, and any cases that were undetermined by these criteria, were reviewed by the consultant in microbiology for the National Blood Authority (Dr John Barbara) who used his own expertise, and consulted with other specialists, to confirm the classification or to determine whether "infectivity", "evidence of an organism" and "no evidence of contamination" were observed in undetermined cases.

Lists of post-transfusion infection reports received were sent six monthly to the reporters. These individuals were asked to check that all infections about which their blood centre had been informed were included on the list, and if not, to report them without further delay.

Additional information about certain cases that were of interest for a specific purpose, or specific period of time e.g. quality assurance data relating

to leucodepletion of components shown to have transmitted bacterial or cell associated infections, was collected from reporters as required

vii) Piloting, and revisions, of the surveillance systems

Pilot

Donation testing surveillance

The provisional surveillance forms were reviewed by the Steering group, the NBS Batch pre-acceptance group (BPAT) and by the microbiology departments at all blood centres, and the forms were revised in the light of the comments received.

The donation testing surveillance system was piloted in five blood centres for the month of August 1995. The five blood centres chosen for the pilot (Brentwood, North London, Leeds, Southampton and Bristol) represented the three geographical and organisational zones of the NBS and also represented the major computer systems in use in blood centres. Minor revisions to the formatting of the forms were made following this pilot month in order to aid completion of the information requested.

Infected donor surveillance and post transfusion infection surveillance

The provisional surveillance forms were reviewed by the Steering group, and by the medical consultants at all blood centres. Completion of the donor surveillance forms from information stored in HCV infected donor files at North London blood centre, and of the post-transfusion infection surveillance forms from information stored in PTI case files at South Thames blood centre was trialed. The forms were revised in the light of the comments received and the experience of their trial use. The forms were introduced for use at blood centres from 1st October for an initial pilot period of six months. Use of the forms continued after the pilot six months without revision.

Revisions

Revisions to Donation testing surveillance during the study period

Electronic reporting

During 1999 and early 2000, reporting on paper forms posted to the surveillance centre was replaced at all English and Welsh centres with

electronic reporting using Microsoft ACCESS and electronic mail. A standard database was designed to receive and manage data at centres and to export data each month to the surveillance centre. Data-entry screens mimicked the paper forms, and reports printed paper copies of the data (again formatted like the paper forms) to be in paper files if necessary. This standard database was customised for each reporting centre to fit their style of data collection (e.g. for daily data-entry or batch data-entry once or twice a month) and to perform local functions (e.g. lists of positive donations for medical follow-up, repeat reactivity rates by week for local test monitoring) in addition to the reporting function. Each centre's database contained all the data reported to date by that centre only. A second much smaller, "transfer" database was also installed at each centre. The data in this database was overwritten by an automatic data export process each month, and this transfer database was copied each month by electronic mail (email) to the NBA. Staff were trained to use the database; run the export and email the transfer database. Any problems or queries after instillation and training were dealt with by telephone by the surveillance co-ordinator who also held a copy of the design of each customised database.

Electronic reporting greatly reduced manual transcription of numbers and test results and reduced data-entry workload - both at the centres where data-entry shortcuts and bar-code readers speeded data-entry, and at the NBA where the bulk of the data was imported directly. The advantages of electronic reporting were greatest for the centres testing largest numbers of donations. The smaller participating centres of the Eire, Northern Ireland, the Channel Isles, and the Isle of Man continued using the paper reporting system.

One revision to the donation testing dataset was introduced into the electronic reporting system. During 1998, nucleic acid testing (NAT) for HCV RNA by PCR was introduced into the testing performed by the blood service. From 1st September 1999, frozen components were released as confirmed HCV RNA negative by pooled PCR testing. At the end of 1999, it was agreed that the donation testing surveillance system should monitor the NAT result for all anti-HCV positive donations.

NAT results

Nucleic acid testing (NAT) results for anti-HCV positive donations were added to the data reported each month at the beginning of 2000. These test results were initially collected retrospectively back to 1st September 1999, to cover the period for which all FFP had been issued as NAT negative. Subsequently data were collected back to 1st April 1999, when NAT testing moved from anonymous pilot testing to testing that resolved results to identified donations. The donation testing databases were modified so that the entry of the result of HCV PCR testing was requested on entry of an anti-HCV positive donation.

Revisions to Infected donor and post-transfusion infection surveillance during the study period

During 1999, following a meeting of all reporters to discuss the surveillance and the use of the data generated by the surveillance systems, the infected donor surveillance forms and the post-transfusion infection surveillance forms were revised (Appendices 6 & 7).

The revisions to the infected donor surveillance forms were: i) prompting for reporting the results of pooled and singleton PCR testing for HCV, ii) a question asking for information about exposures to be summarised as either a.) Donor has no identified risk despite satisfactory follow-up information available, b.) Risk for the donor not identified, possibly because of incomplete follow-up information, or c.) One or more probable risk factor identified, with the details of each risk factor only completed for those in group c), iii) revision of the risk factor grid to separate donors exposures from donor's heterosexual partner's exposures, and iv) a question asking (of group c.) donors) why the donor did not disclose the existing risk factor at the time of donating blood, instead of the question asking for the method by which the information on the report had been obtained.

The revisions to the post-transfusion infection surveillance forms were i) provision to specify that the report referred to a post-transfusion reaction suspected to be due to bacteria (rather than a confirmed bacteraemia), ii) alternative versions of the section 2 and 3 forms specific for post-transfusion bacteraemias and post-transfusion reactions suspected to be due to bacteria. These alternative forms (PTI(bac)) included questions on the age of the

component, the method of platelet collection, the method of any leucodepletion performed on the component and allowed more space for free text to describe the source of the samples available for culture and the investigations conducted on these samples.

viii) Co-ordination with laboratory reports to PHLS-CDSC

Co-ordination of reports to other specific infection surveillance systems

Blood centres were advised that with the introduction of the NBA/PHLS-CDSC surveillance system they were no longer requested to complete separate HIV antibody positive report forms, or HBsAg positive report forms, for the PHLS-CDSC. From the 1st October 1995 these reports for the PHLS-CDSC infection specific surveillance systems were generated from the NBS/PHLS-CDSC system using the information reported on the IDS and the PTIS forms.

The PHLS-CDSC HIV/AIDS surveillance centre sometimes receives further information about an HIV infected blood donor when the individual attends for care at another centre (usually a genitourinary medicine clinic), or when the individual is diagnosed with AIDS, or dies. This information is provided in confidence by voluntary reporters. The PHLS-CDSC HIV/AIDS centre also conducts follow up of individuals, including blood donors, who have no identified risk for HIV infection, or report only heterosexual contact in the UK with partners who have no known high-risk exposure. The PHLS-CDSC HIV/AIDS centre therefore may hold information about blood donors that is not known to the blood centres were the donors were tested. Periodically (quarterly from October 1995-December 1996 and six-monthly from January 1997), the NBA/PHLS-CDSC surveillance system cross checked reported information for HIV positive donors with the PHLS-CDSC HIV/AIDS centre, and the most up to date information was obtained. Information obtained from PHLS-CDSC HIV/AIDS centre was held separately to information reported by blood centres and was not communicated to blood centres except without any means of donor identification in summary tables.

The PHLS-CDSC HIV/AIDS centre informed the NBA/PHLS-CDSC surveillance system of any newly reported HIV positive individuals with transfusion in the UK reported as the suspected route of infection.

The PHLS-CDSC Hepatitis section informed the NBA/PHLS-CDSC surveillance system of any individuals reported with acute HBV infection with transfusion in the UK as a suspected route of infection, and of any anti-HCV positive report with transfusion in the UK since September 1991 (i.e. the start of anti-HCV testing of all blood donations) as the most probable route of infection.

In 1995, when many individuals who received transfusions prior to the introduction of anti-HCV testing of blood donations were requesting anti-HCV testing to investigate their infection status, the PHLS-CDSC Hepatitis section conducted a survey of the numbers of anti-HCV tests performed at PHLs and the reasons for testing and test results. Reports of infected recipients with a history of transfusion in England prior to testing were passed to the National Blood Service. These infections, probably acquired from untested anti-HCV positive transfusions, were excluded from the surveillance of post-transfusion infections and have been collated elsewhere (National Lookback Collaborators, 2001).

PHLS colleagues working on surveillance of specific organisms that may be transfusion transmissible were made aware of the NBA/PHLS-CDSC transfusion transmissible infection surveillance project and asked to pass on any relevant infection reports.

Interrogation of LABBASE

Public Health Service laboratories (PHLs), National Health Service laboratories and some private laboratories routinely report all detected infections to PHLS-CDSC Lab-Base.

Transfusion was not, during this time, included as a coded feature for any infections reported by laboratories to PHLS-CDSC Lab-Base. Infections that were, or might have been, associated with transfusion could therefore be identified only by searching a free-text field ("comments") for any mention of transfusion. Due to variation in both the completeness of infection reporting and the amount of information included on reports from different laboratories, analysis of clinical or epidemiological data provided with routine reports to CDSC Lab-base must be considered with caution.

Two investigations of reports to Lab-Base were conducted. Firstly, in July 1995, two selections were made from reports received by CDSC between the beginning of 1994 and week 27 of 1995. The first selection was of reports of bacteraemias with comments mentioning transfusion. Examination of the comments showed that for 40% (19) of these selected reports, there was no indication of infection associated with blood transfusion. For 3 isolates from 2 patients, comments indicated that the bacteraemia was definitely associated with transfusion. Both these cases had been investigated by the NBS. The remaining 29 isolates were concluded to represent possible cases of transfusion associated bacteraemia. The second selection was of a subset of organisms reported to Lab-Base. Organisms that were likely to be isolated from blood cultures relatively infrequently (<500 reports per year) and which might be transfusion transmissible were selected. 83 selected organisms (including *Yersinia enterocolitica* (23), *Pseudomonas fluorescens* (53), *Pseudomonas putida* (18), *Pseudomonas cepacia* (43), *Serratia marcescens* (269) and *Serratia liquifaciens* (96)) yielded 2,966 reports. Review of the contents of the free text fields suggested that, when the underlying clinical condition reported was one for which transfusion would almost certainly have been required, a history of transfusion had rarely been reported.

This pilot examination of Lab-Base led to a request for history of transfusion (yes/no) to be included as a standard prompted feature for selected organisms in future developments of the Lab-Base system so that selection of infections which may be associated with transfusion may be performed more accurately. Subsequent changes to the Lab Base system and methods of reporting have decreased the free text information reported and further use of this system has not been developed.

A second attempt to interrogate Lab-Base for information about transfusion-transmitted infections was made in 2000 when information was needed about CMV transmission by transfusion - particularly to neonates. All laboratory reports of CMV infection to CDSC (LABBASE) were queried for relevant information. As for bacterial infections, information about recent transfusion is not routinely requested for CMV infection reports: a free text field is available for reporters to note comments of possible relevance.

Of 2,925 CMV infections reported to LABBASE from 1/1/97 to date, 101 (3.5%) were in patients known to be less than 3 weeks of age. Fifty of these babies had comments associated with their CMV report - no comments mentioned transfusion. Of all 2,925 reports, 1,269 had comments and 5 of these mentioned transfusion:-

1. (Wk: 9717) 3-5 month old male baby, comment: preterm/jaundice/blood transfusion (N.B. Not the same case as the one reported to a blood centre during 1997.).

2. (Wk: 9836) 29 yr old female transplant recipient, comment: blood transfusion

3. (Wk: 9832) 54 yr old male, comment: H/O transfusion

4. (Wk: 9701) 57 yr old female, comment: thought to be from blood transfusion in Egypt

5. (Wk: 9813) 73 yr old male, comment: post transfusion

The three LABBASE reports during 1998 (9836, 9832, 9813) that mention transfusion were, according to information from blood centres, not reported to the blood services for investigation. This may be due to identification of another source of infection or under-reporting to the blood service.

Lab reports of infections in babies had comments more frequently than reports of infections in older aged patients.

No evidence was found of transfusion associated CMV cases during 1998/99. Four of 2,925 (0.14%) laboratory reports of CMV infection (1997 to date) mentioned a history of transfusion not known to have been abroad, but these do not seem to have been investigated by blood services.

As blood centres may not be informed of suspected post-transfusion CMV infections, and laboratory reports to CDSC do not routinely contain information about whether or not the patient has had a recent transfusion, the available data could not demonstrate there had been no such cases. Further follow up of selected LABBASE reports may be worthwhile if further work on this issue is required. As transfusion associated CMV cases in babies are of most importance, and reports for this group were also more detailed, a routine search of LABBASE for CMV cases in babies that mention transfusion in the comments, with follow up of any cases via the reporter, was considered, but has not been carried out.

ix) Routine reports of collated data from the surveillance centre

Donation testing surveillance data were collated monthly and a tabular report of the reactivity rates for the past month, and the confirmed infection rates for the last-but-one month, was sent to all blood centres and other interested centres by the 25th of the next month. The output from the monthly analysis of donation testing data where circulated to key staff overseeing donation testing and quality assurance. (Appendix 6 contains the report for September 1999 with centre and manufacturer names removed.)

Up until December 1996, data from the infected donor surveillance and post-transfusion infection surveillance systems were collated by calendar quarter and a tabular and graphical report (NBA/PHLS CDSC Infection Surveillance report) was sent to all blood centres and other interested centres at the end of the following calendar quarter. From January 1997, the frequency of infection surveillance reports was changed to be six monthly (Appendix 7 contains Report 10, with data to end June 1999).

The content and analyses included in these routine reports is described below.

3.2 Results

Donation testing

Between 1/10/95 and 30/09/99, 11,442,706 blood donations were tested by the blood services of England, Wales, Northern Ireland, the Channel Isles and Isle of Man and the Republic of Ireland and the results of testing these donations for HBsAg, anti-HCV, anti-HIV and Treponemal antibodies were reported to the surveillance system.

Appendix 6 shows the monthly report for September 1999. This report presents data on donations tested during September 1999, and cumulatively since October 1995. Tables 2a, 2b and 1c from the October 1999 report are also included in appendix 6: these tables show the confirmed positives during September 1999 and cumulatively from October 1995 to September 1999.

(Note: Manufacturers' and products' names and centre names have been blanked-out of the tables included in this thesis, as some of these data are confidential.)

Table 3.3 and Figure 3.3 summaries the specificity of the assays used over this period - according to the data reported.

Table 3.3 Summary reactivity to screening tests for HBsAg, anti-HCV, anti-HIV and T.pallidum antibodies: batches in use September 1999
All donations reported to NBA/PHLS CDSC Donation testing surveillance, 01/10/95 to 30/09/99 (4 years)

Test Kit (3 with highest usage, and others)	***Number tested***	***Number repeatedly reactive***	**%**	***Number confirmed positive***	***Falsely repeatedly reactive***
HBsAg					
Test 1 (i.e. most used)	518,381	439	0.085%	11	0.083%
Test 2	262,443	30	0.011%	10	0.008%
Test 3	130,996	205	0.156%	4	0.153%
Others	29,218	19	0.065%	0	0.065%
All test kits	941,038	693	0.074%	25	0.071%
Anti-HCV					
Test 1	259,004	235	0.091%	15	0.085%
Test 2	151,846	55	0.036%	4	0.034%
Test 3	66,602	39	0.059%	10	0.044%
Others	22,629	18	0.080%	0	0.080%
All test kits	500,081	347	0.069%	29	0.064%
Anti-HIV					
Test 1	344,895	168	0.049%	2	0.048%
Test 2	251,820	203	0.081%	4	0.079%
Test 3	144,762	68	0.047%	1	0.046%
Others	8,564	5	0.058%	0	0.058%
All test kits	750,041	444	0.059%	7	0.058%
T.pallidum					
Test 1	547,887	154	0.028%	12	0.026%
Test 2	68,502	33	0.048%	1	0.047%
Test 3	52,521	15	0.029%	1	0.027%
Others	43,706	53	0.121%	0	0.121%
All test kits	712,616	255	0.036%	14	0.034%
All test kits, all markers					0.227%
Test 1, all markers	58%				0.242%

Figure 3.3 False reactivity: most commonly used kits, others, and all tests

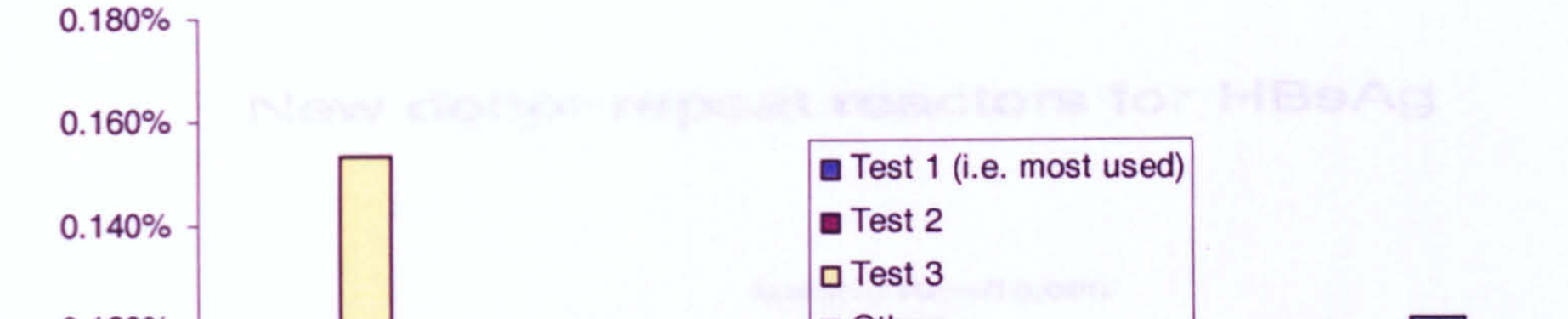
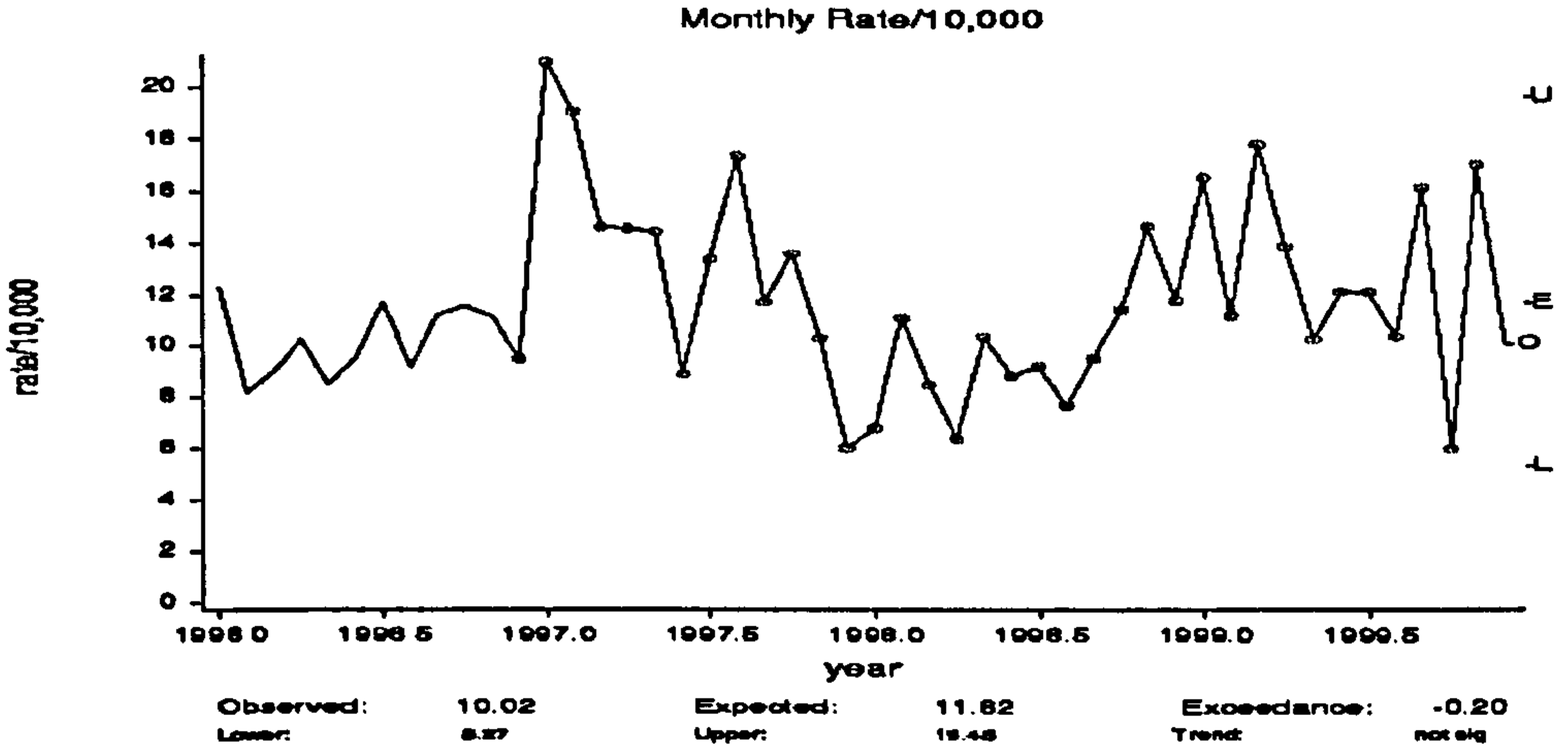


Figure 3.4 show the rates of repeat-reactivity and of confirmed markers of infection over the four-year period 01/01/96 to 30/09/99, for donations from new donors, donations from repeat donors and for all donations.

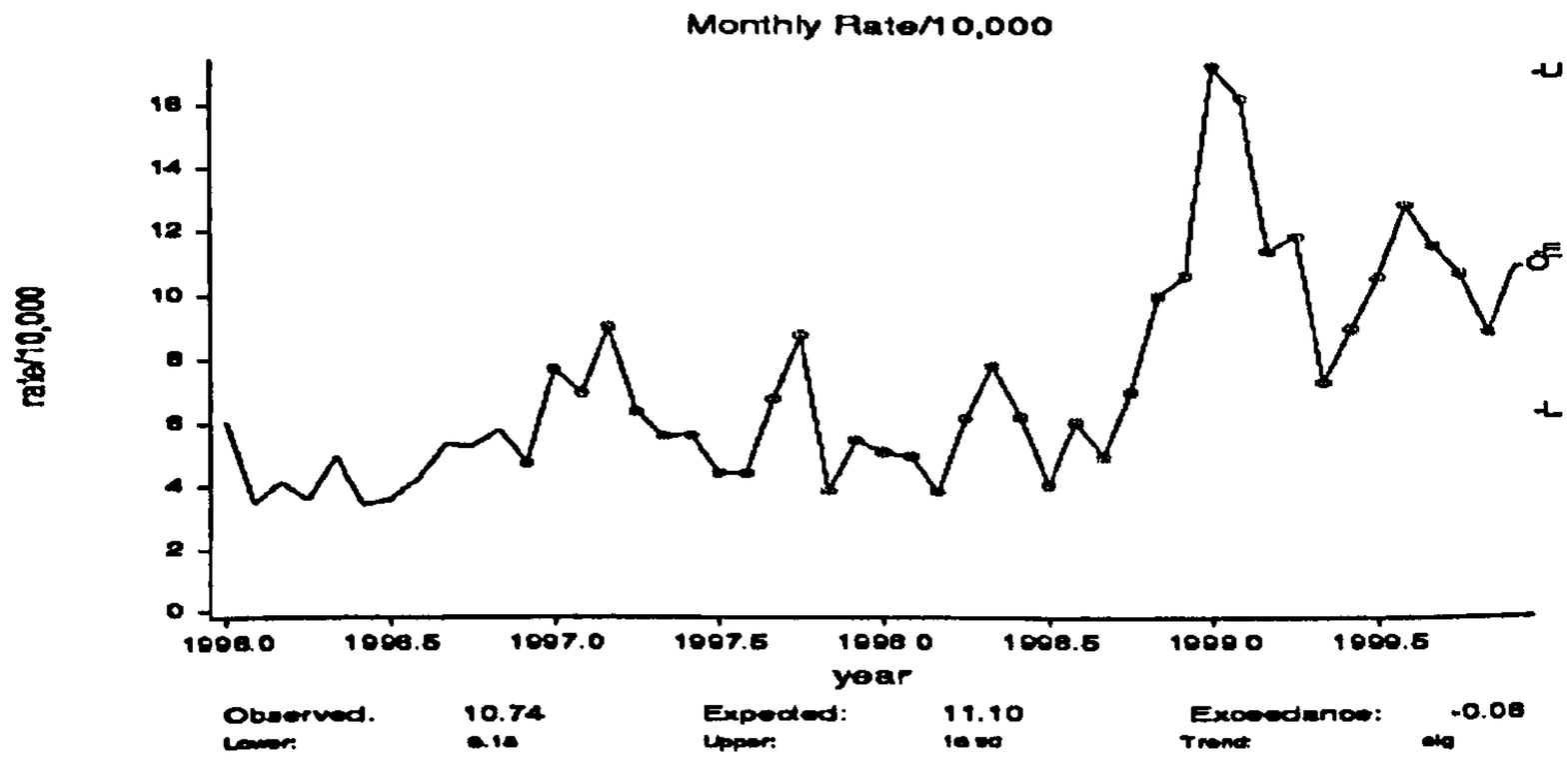
Figure 3.4 Frequency per 10,000 donations of reactivity and confirmed positivity for HBsAg, anti-HCV, anti-HIV and Treponemal antibodies for donations from new donors, donations from repeat donors and all donations, 1996-1999.

(See graphs on next twelve pages.)

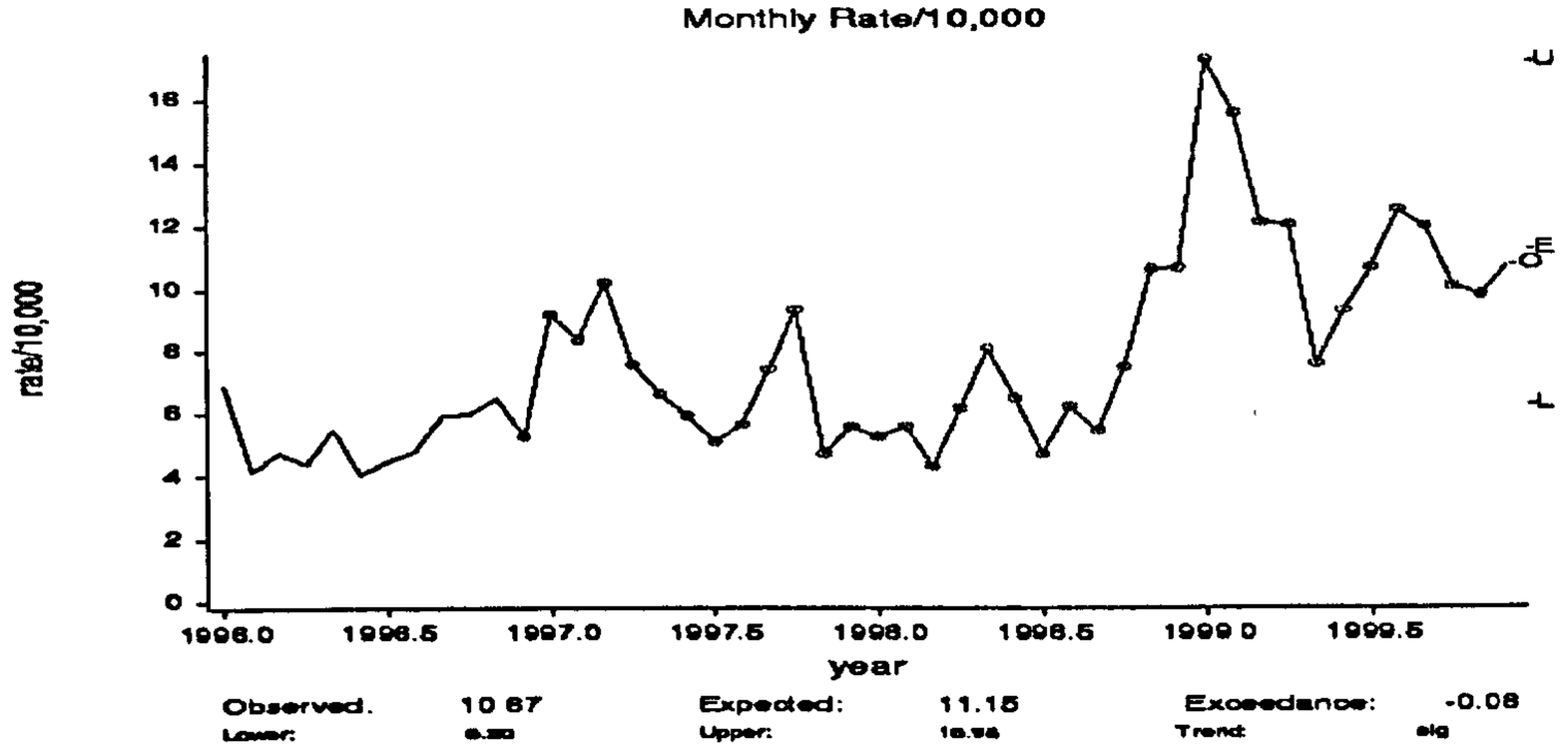
New donor repeat reactors for HBsAg



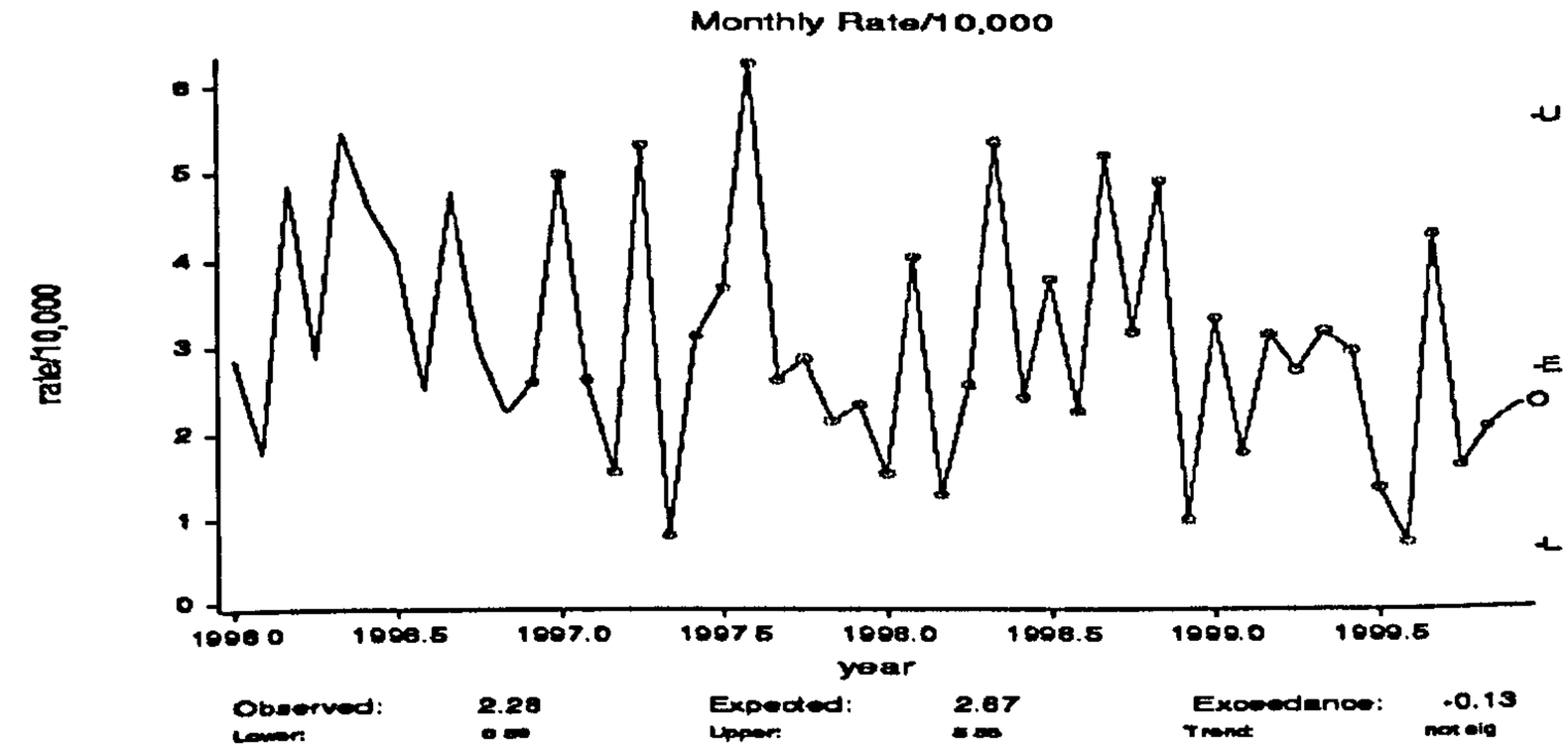
Old donor repeat reactors for HBsAg



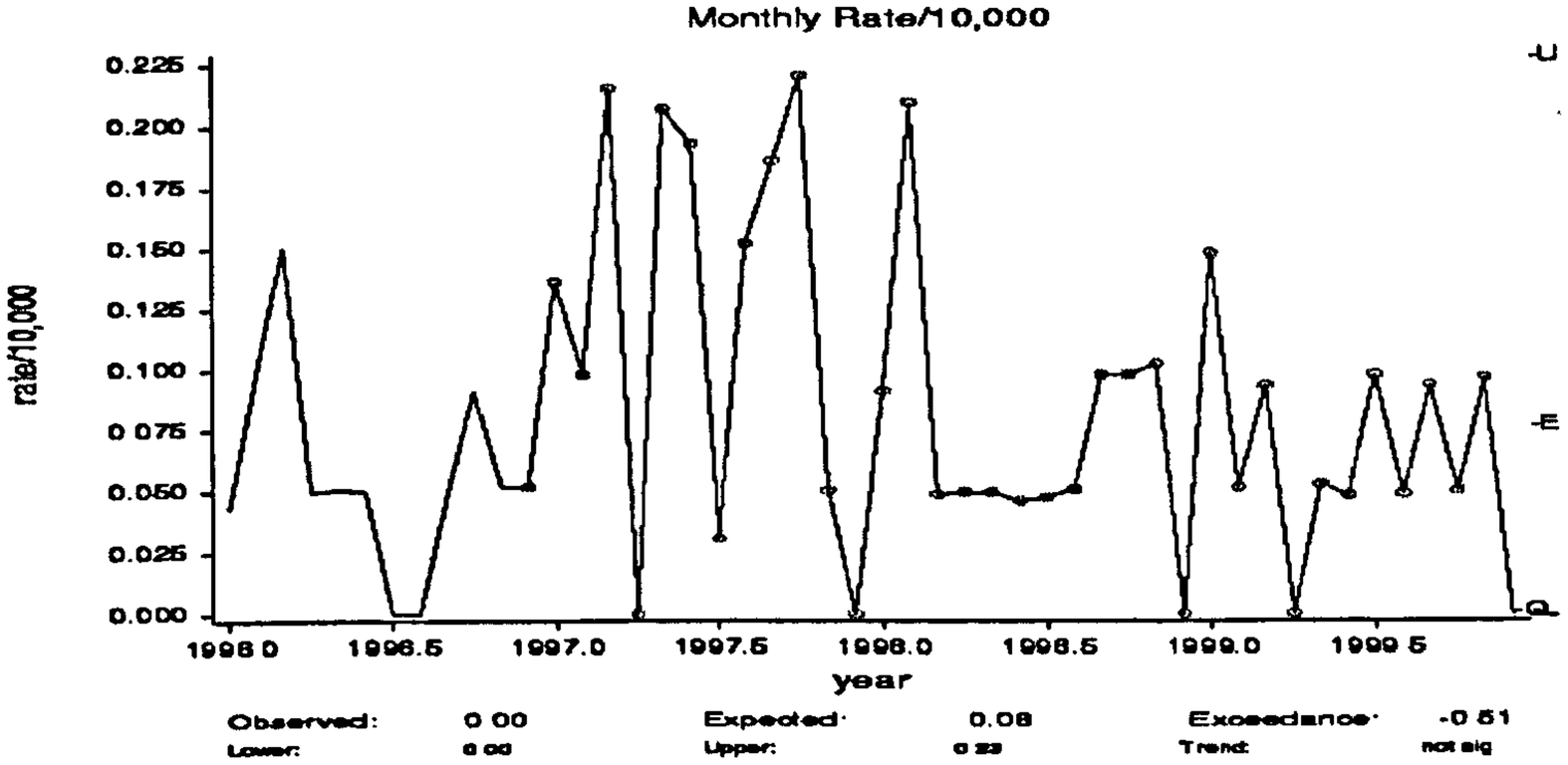
All donor repeat reactors for HBsAg



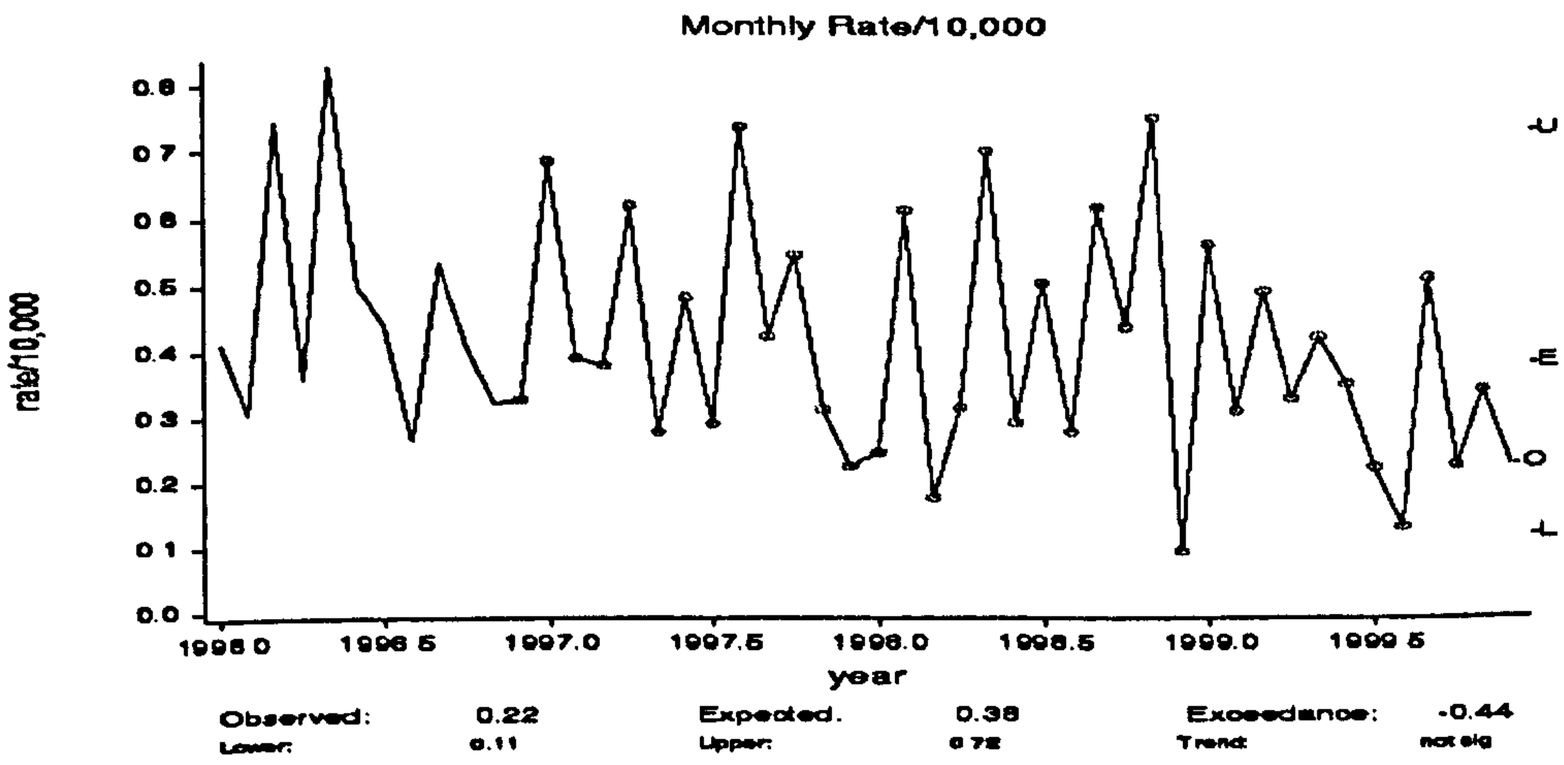
New donor Infections for HBsAg



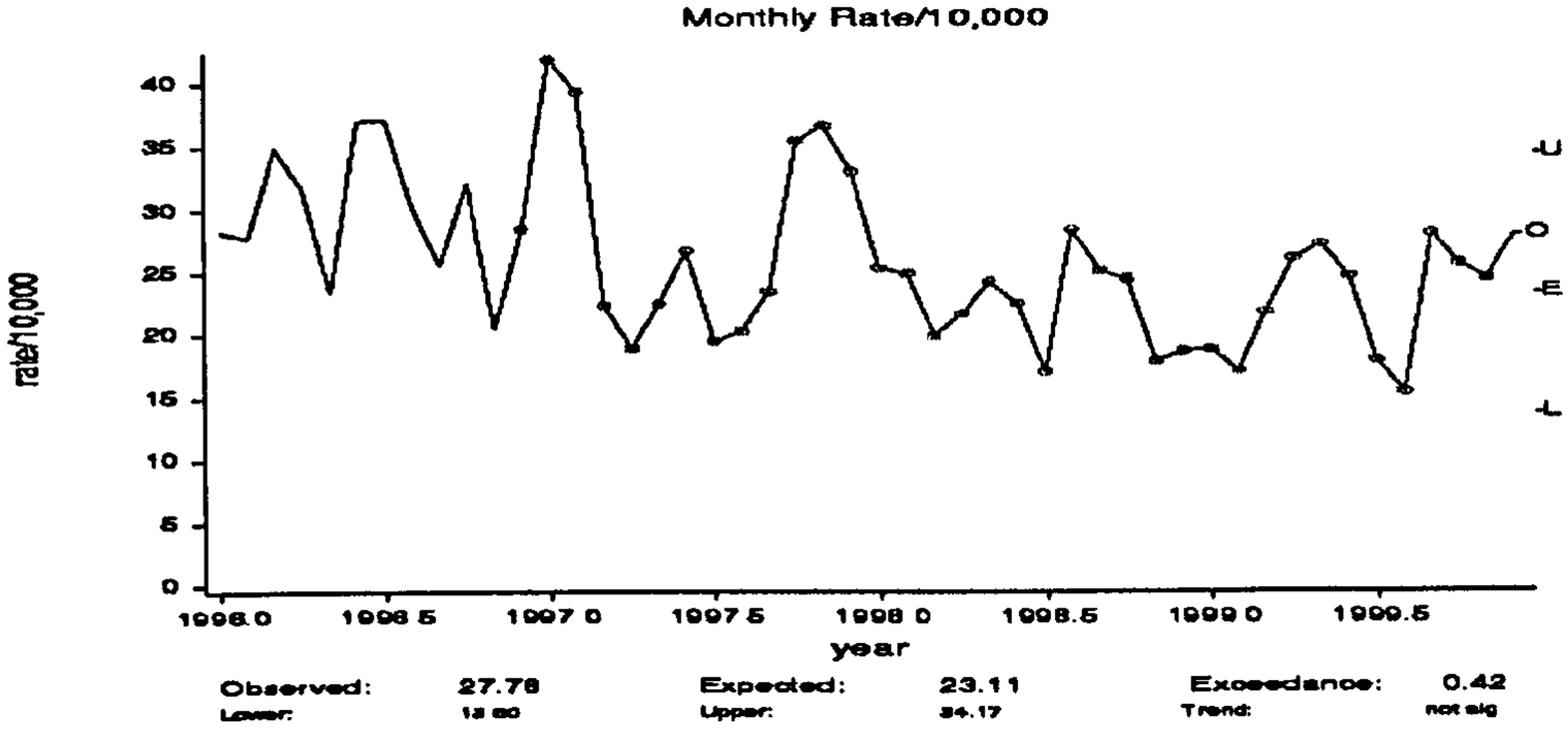
Old donor Infections for HBsAg



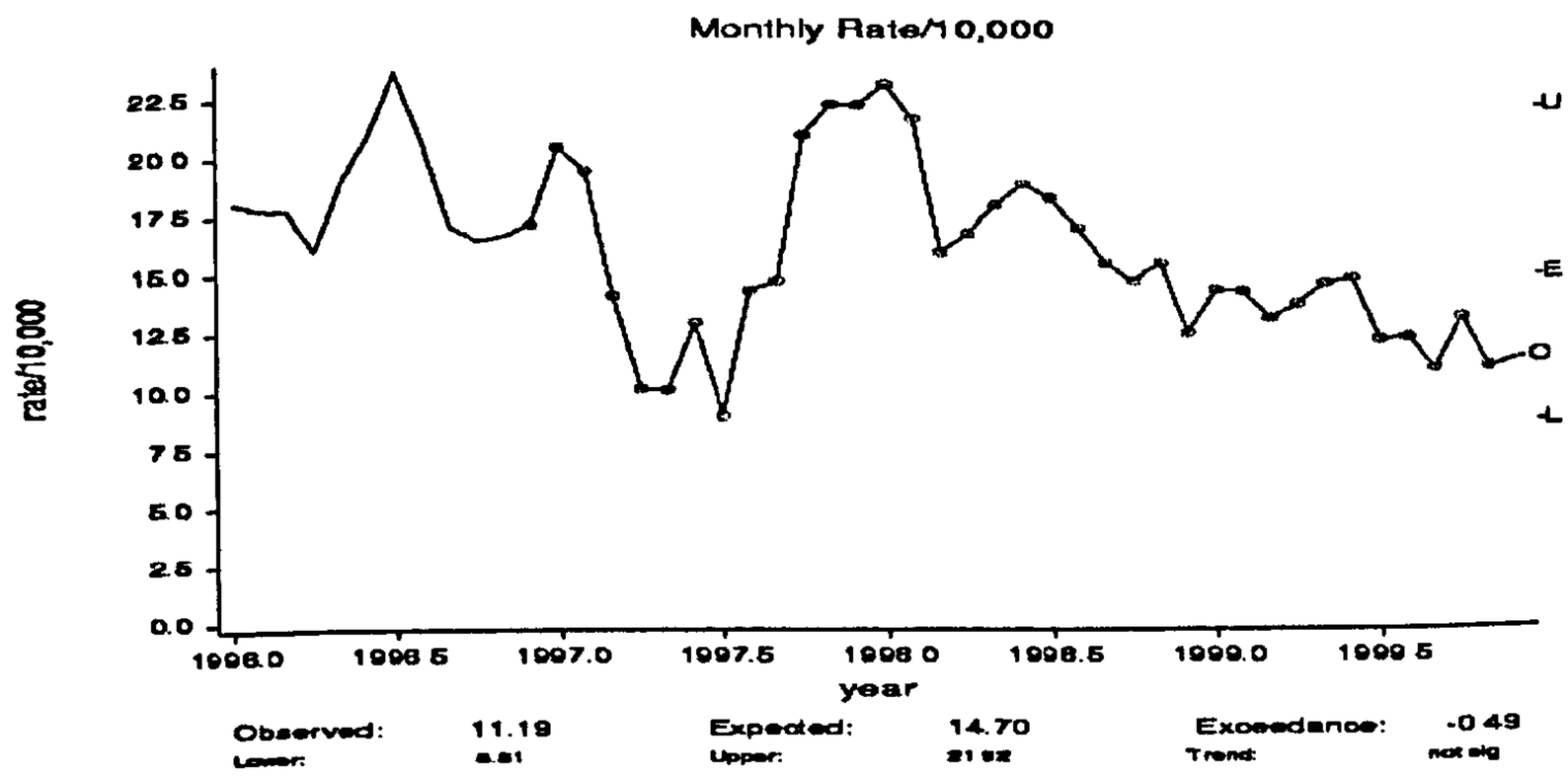
All donor Infections for HBsAg



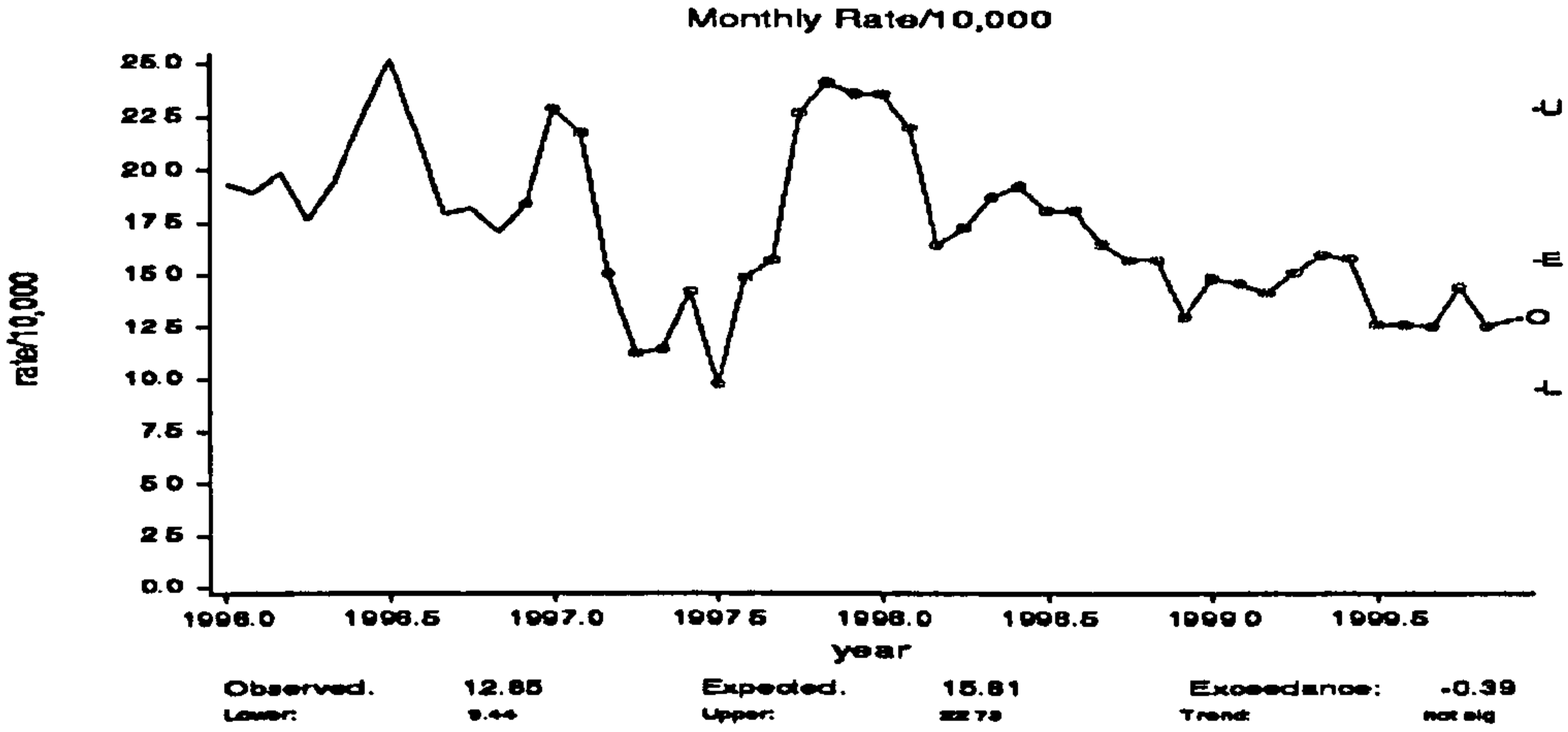
New donor repeat reactors for anti-HCV



Old donor repeat reactors for anti-HCV

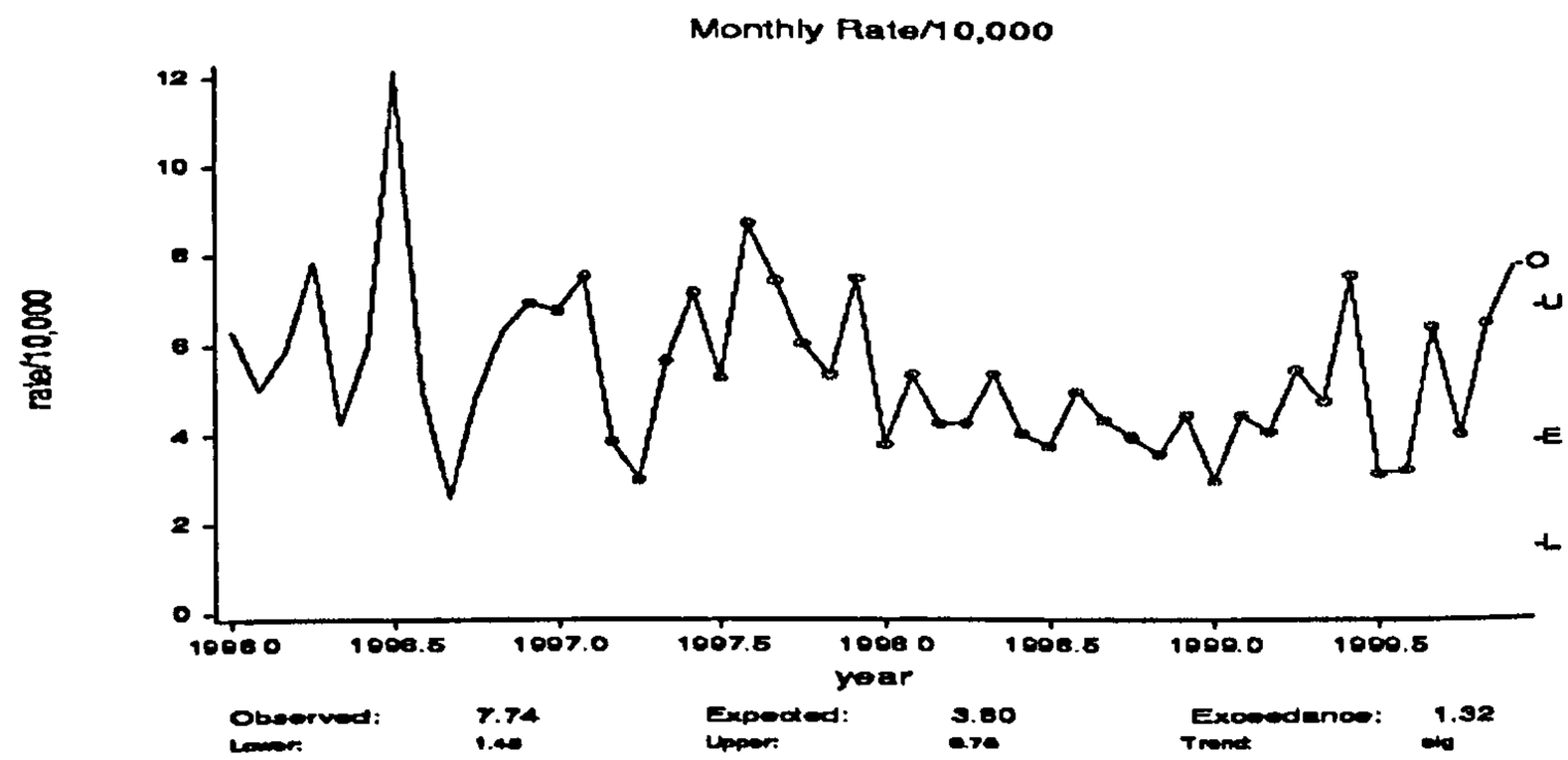


All donor repeat reactors for anti-HCV



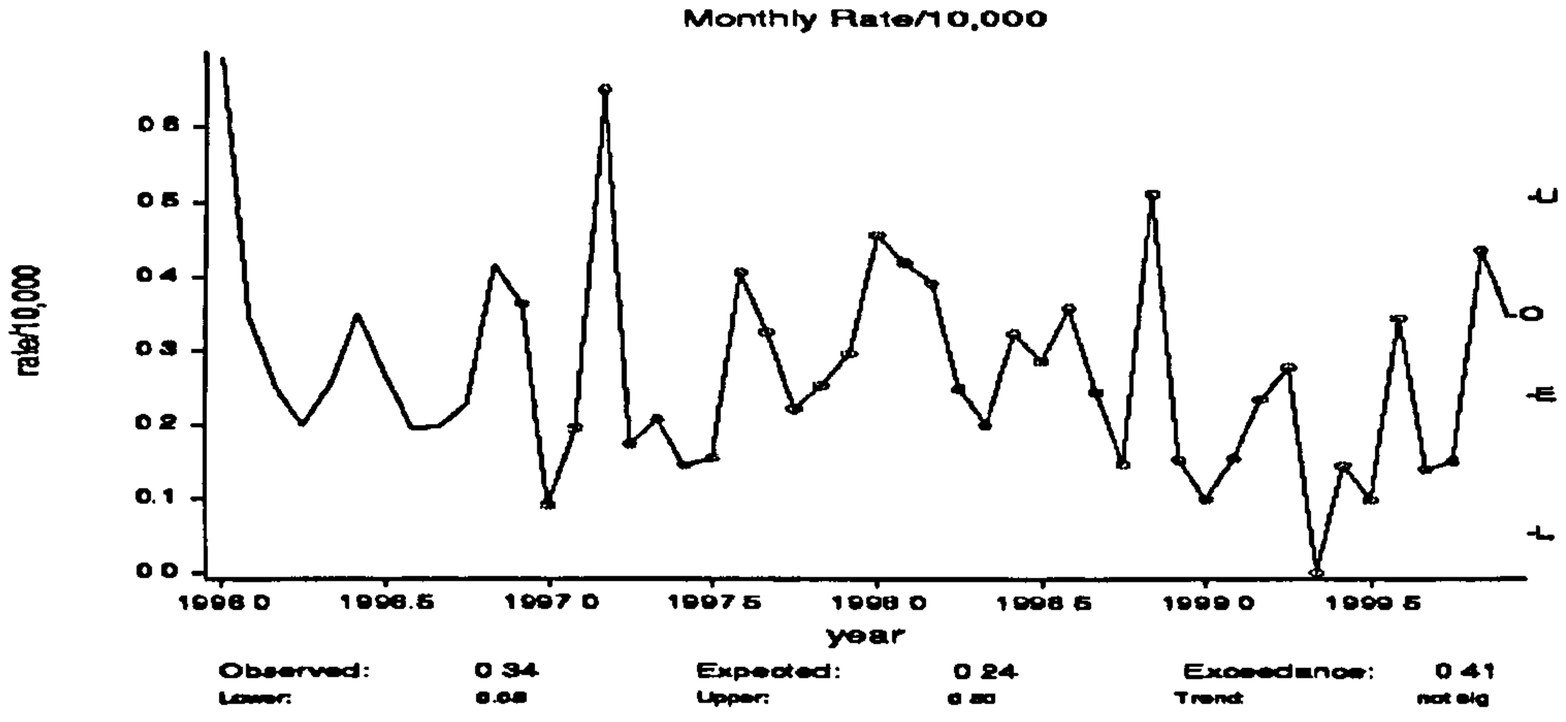
Observed. 12.85 Expected. 15.61 Exceedance: -0.39
Lower: 9.44 Upper: 22.79 Trend: not sig

New donor Infections for anti-HCV

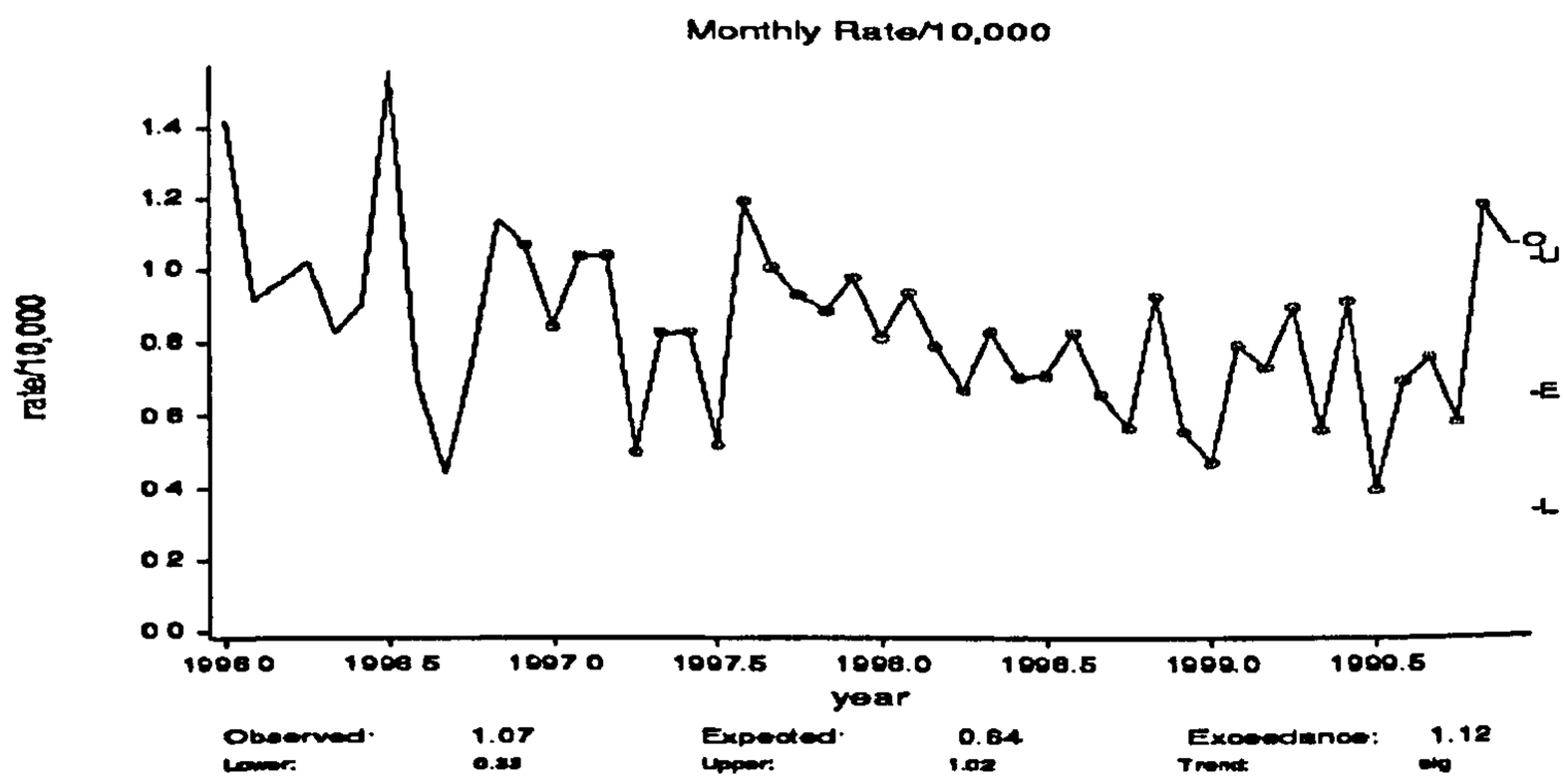


Observed: 7.74 Expected: 3.80 Exceedance: 1.32
Lower: 1.48 Upper: 8.78 Trend: sig

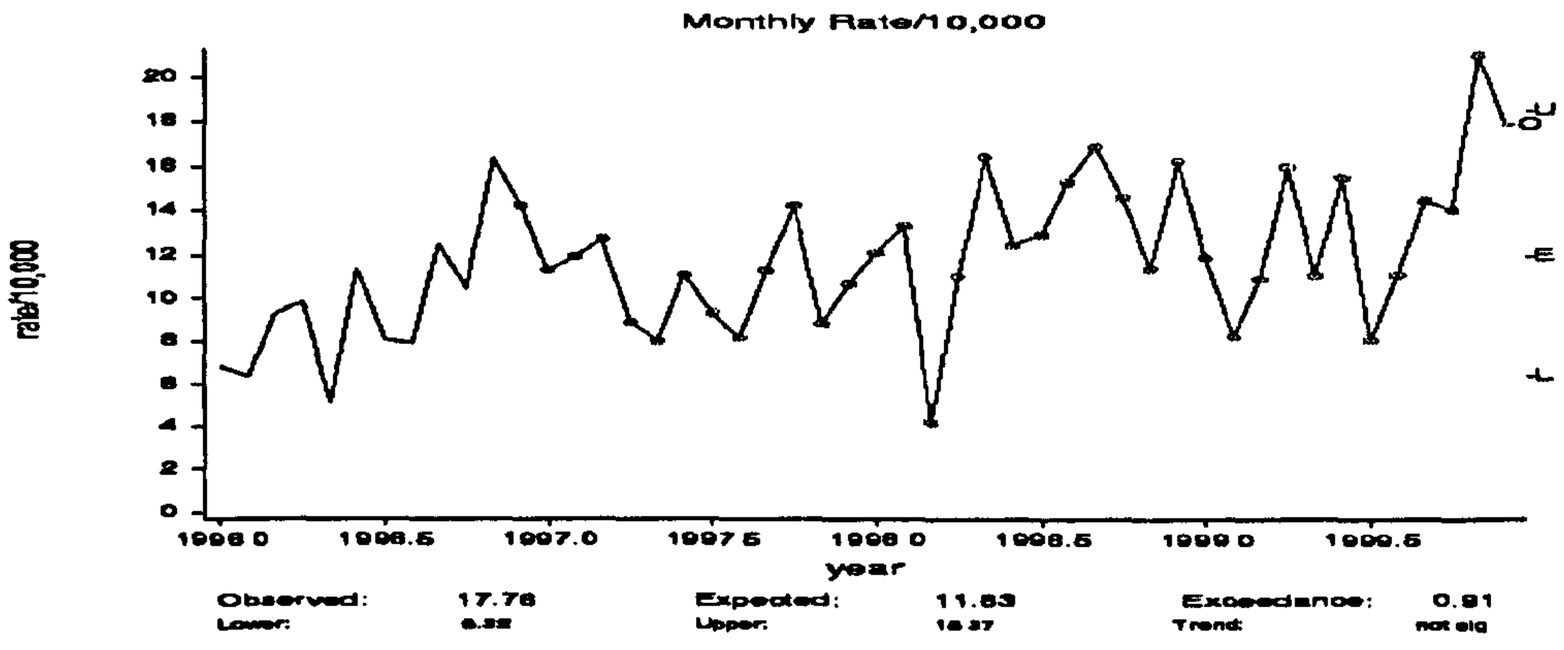
Old donor Infections for anti-HCV



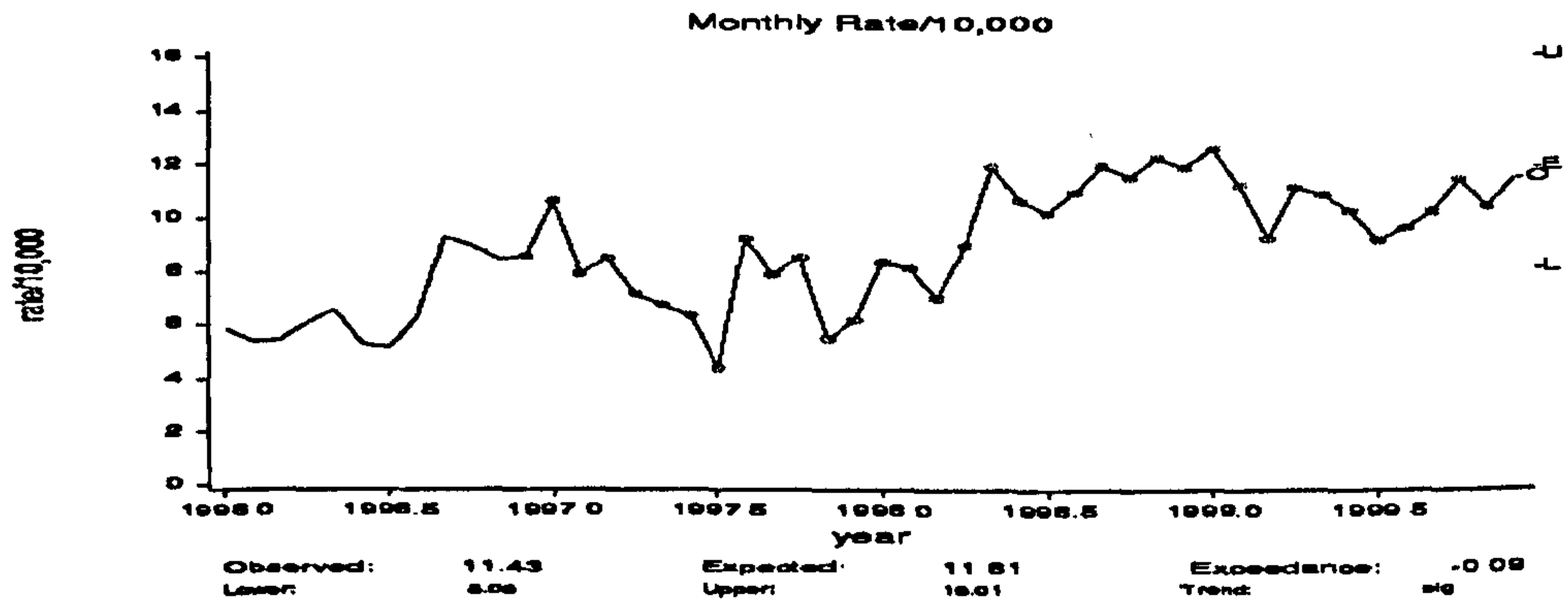
All donor Infections for anti-HCV



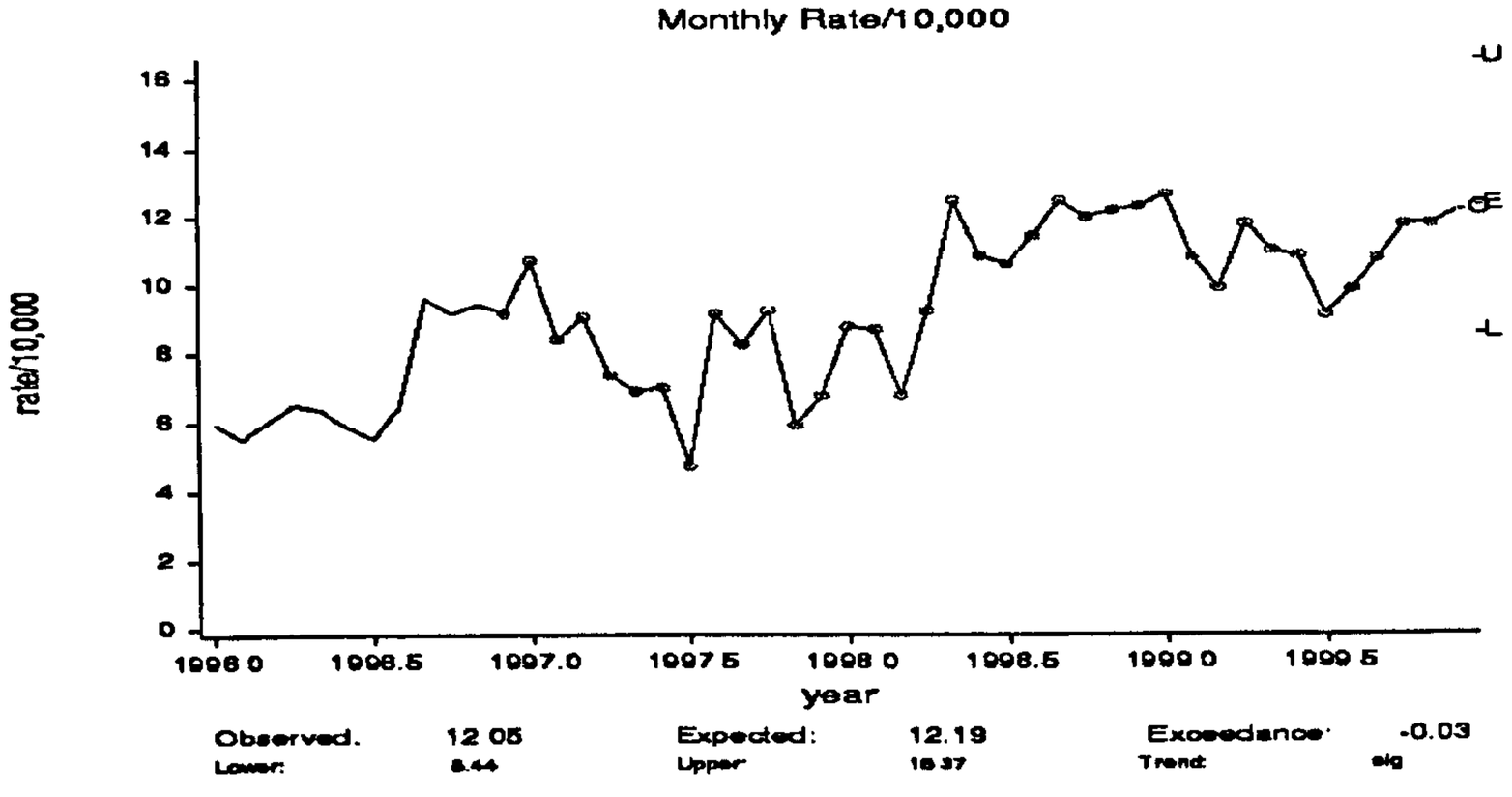
New donor repeat reactors for anti-HIV



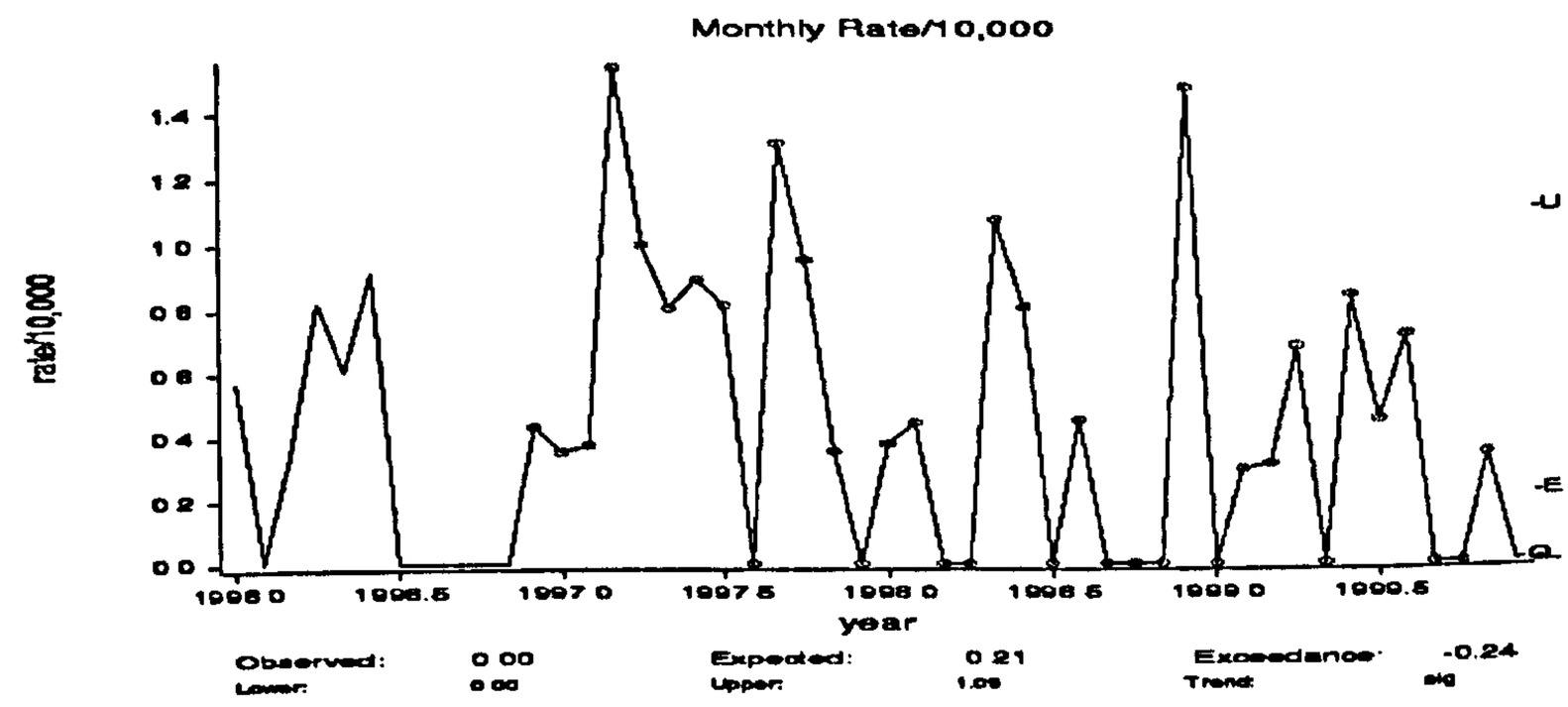
Old donor repeat reactors for anti-HIV



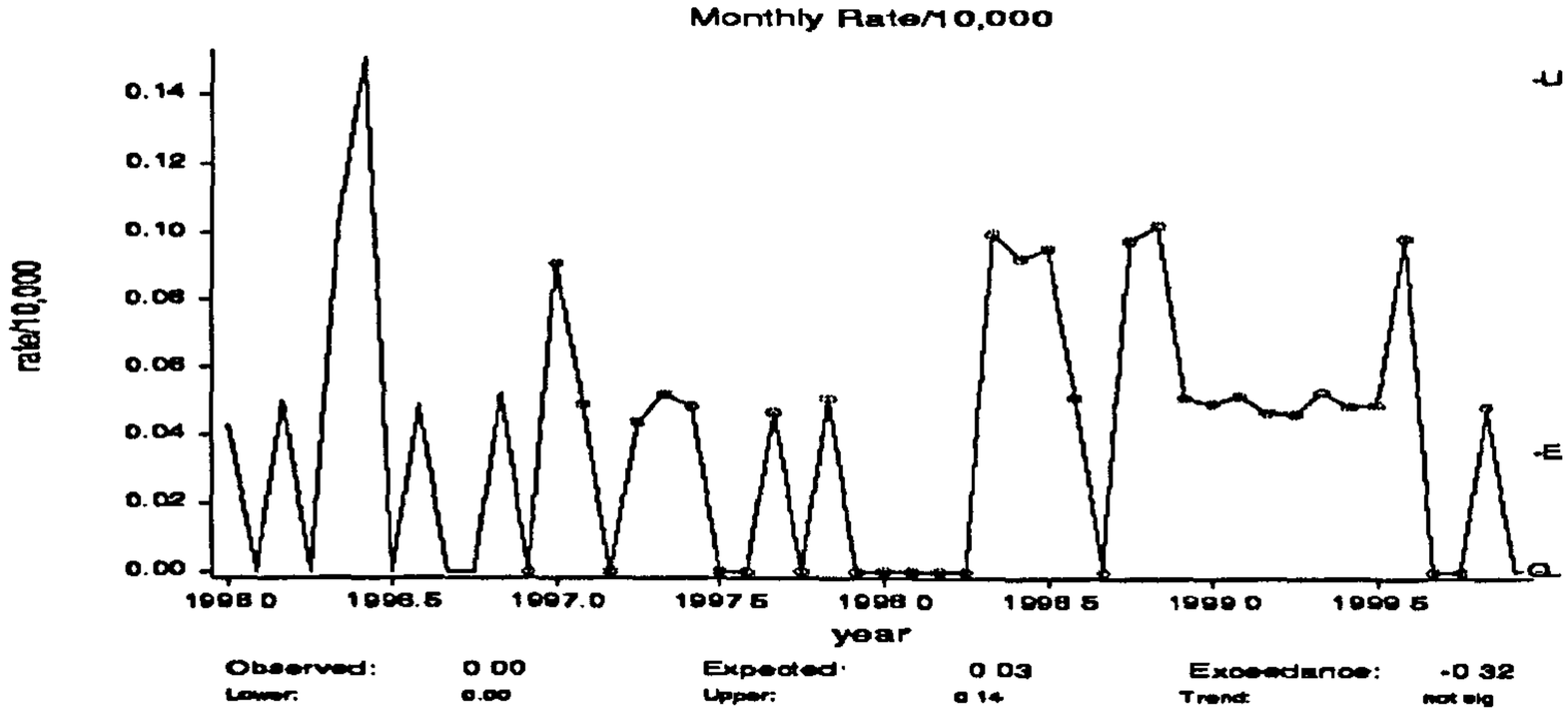
All donor repeat reactors for anti-HIV



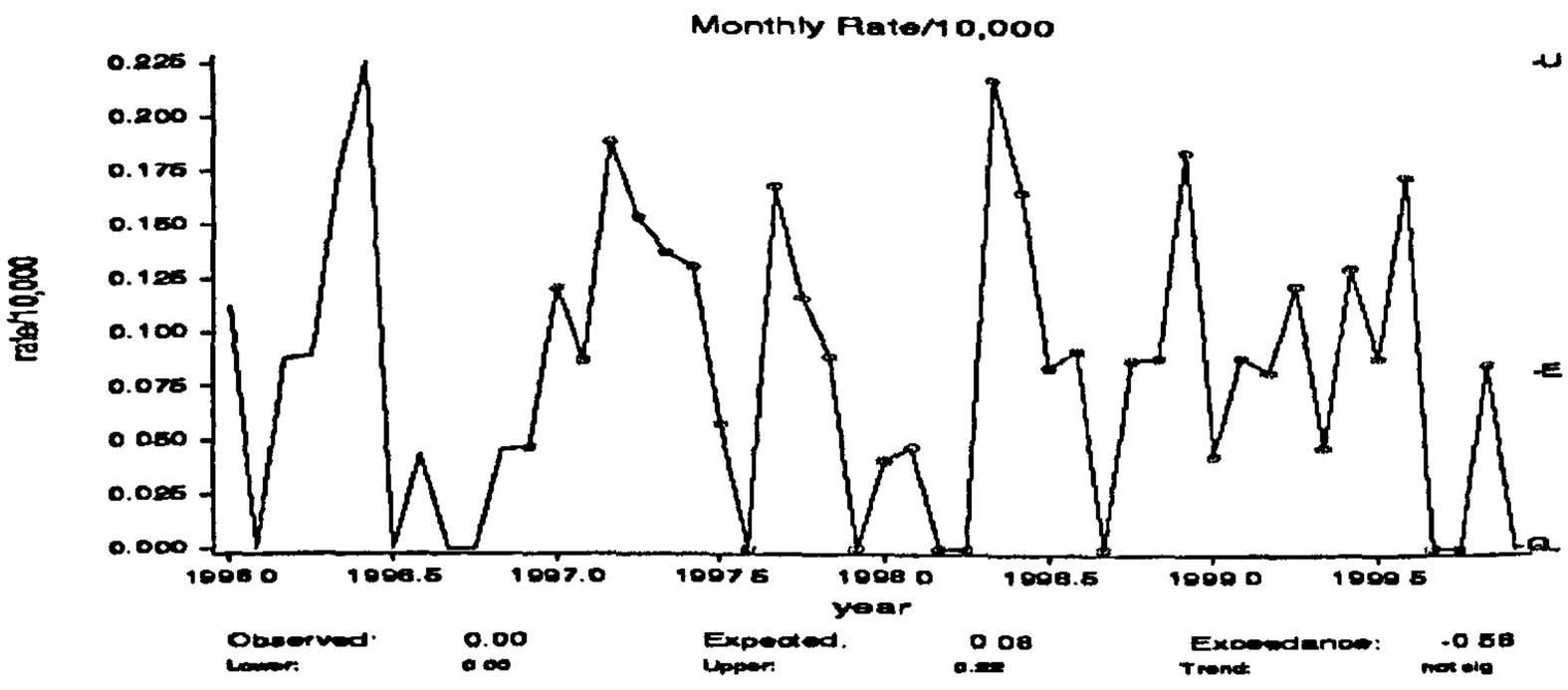
New donor Infections for anti-HIV



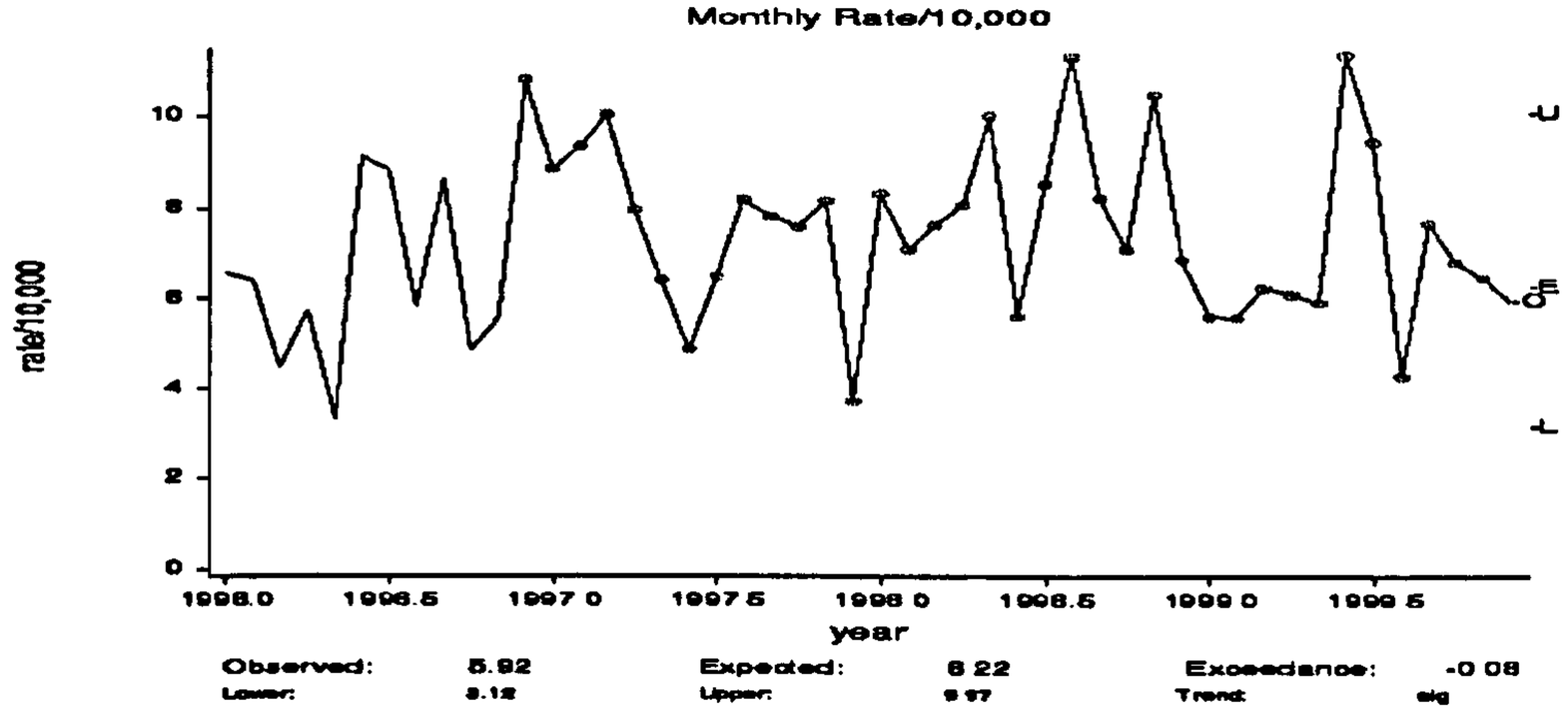
Old donor Infections for anti-HIV



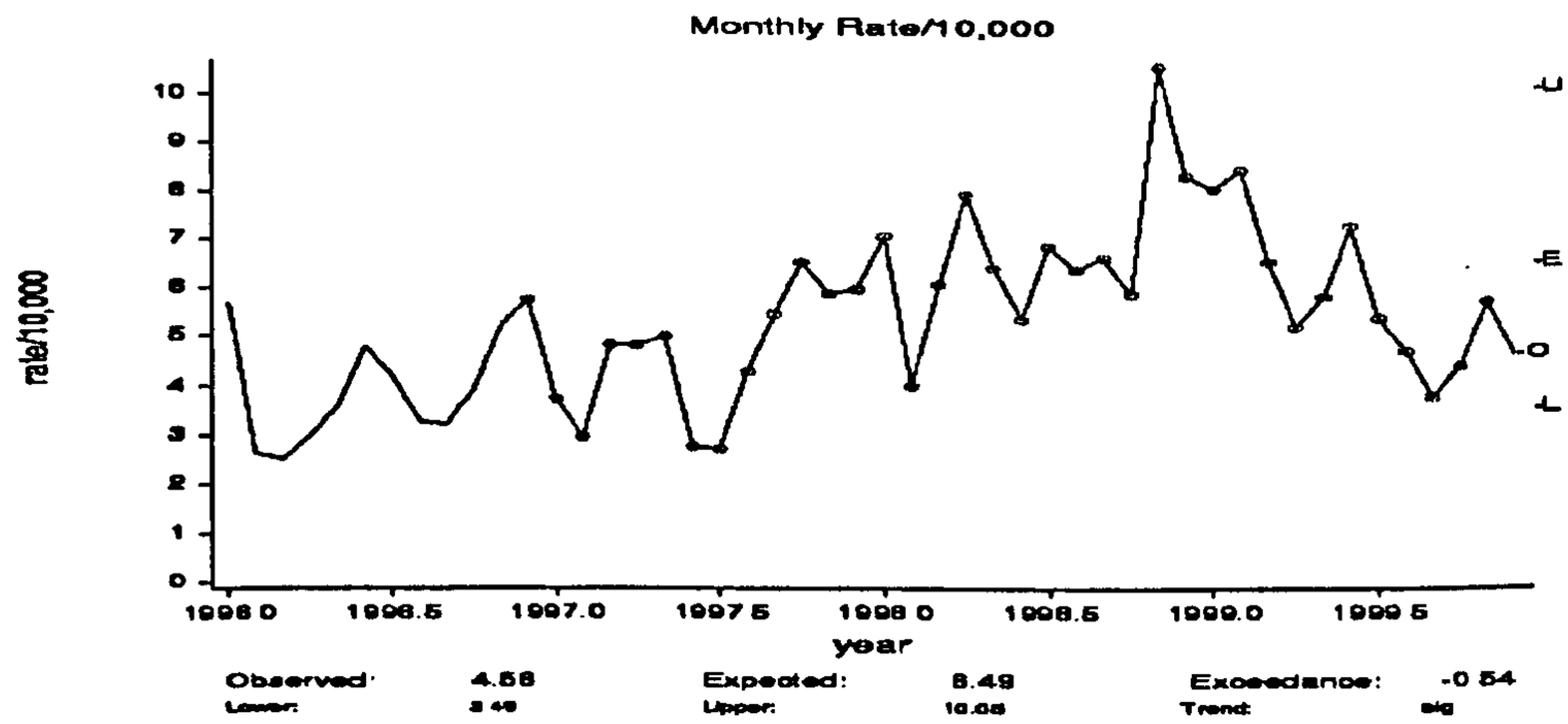
All donor Infections for anti-HIV



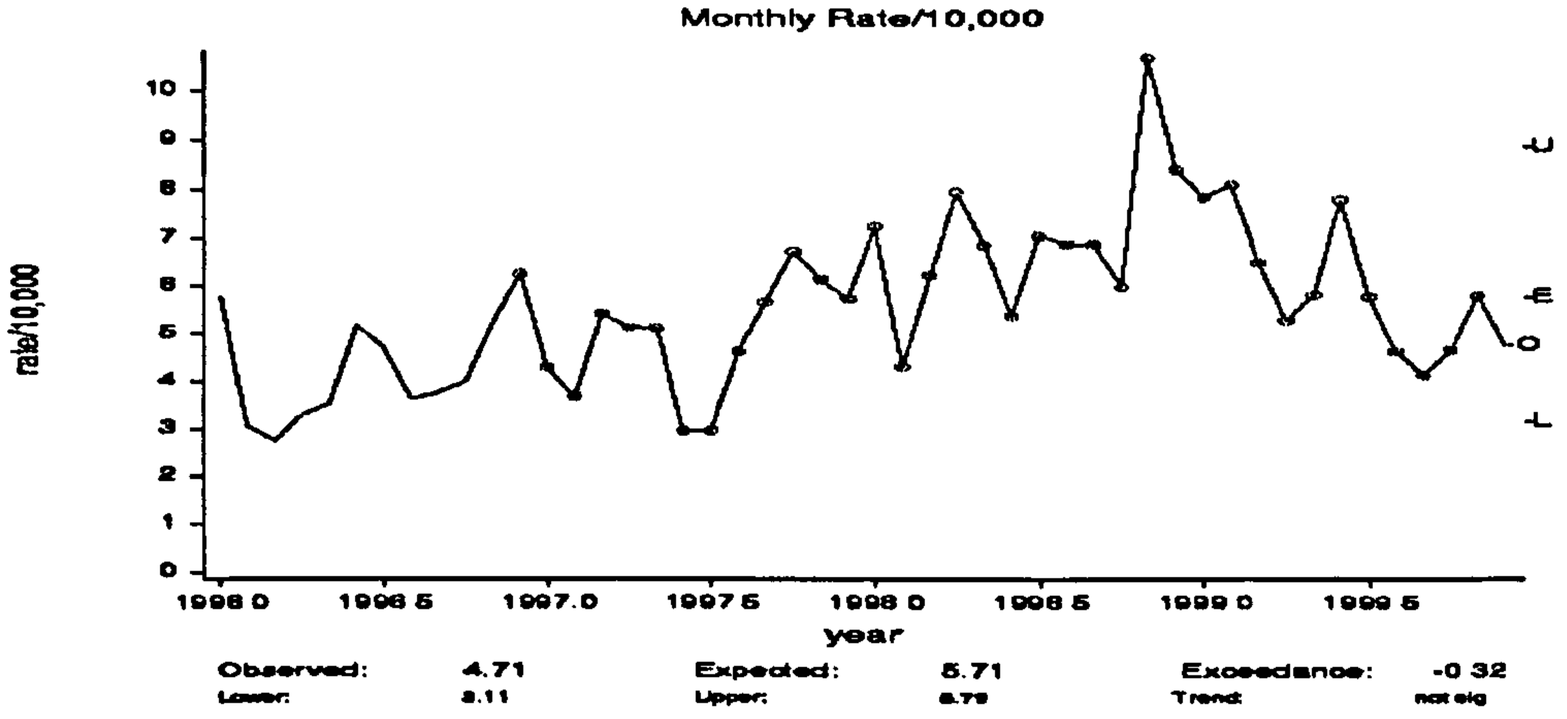
New donor repeat reactors for T.pallidum antibodies



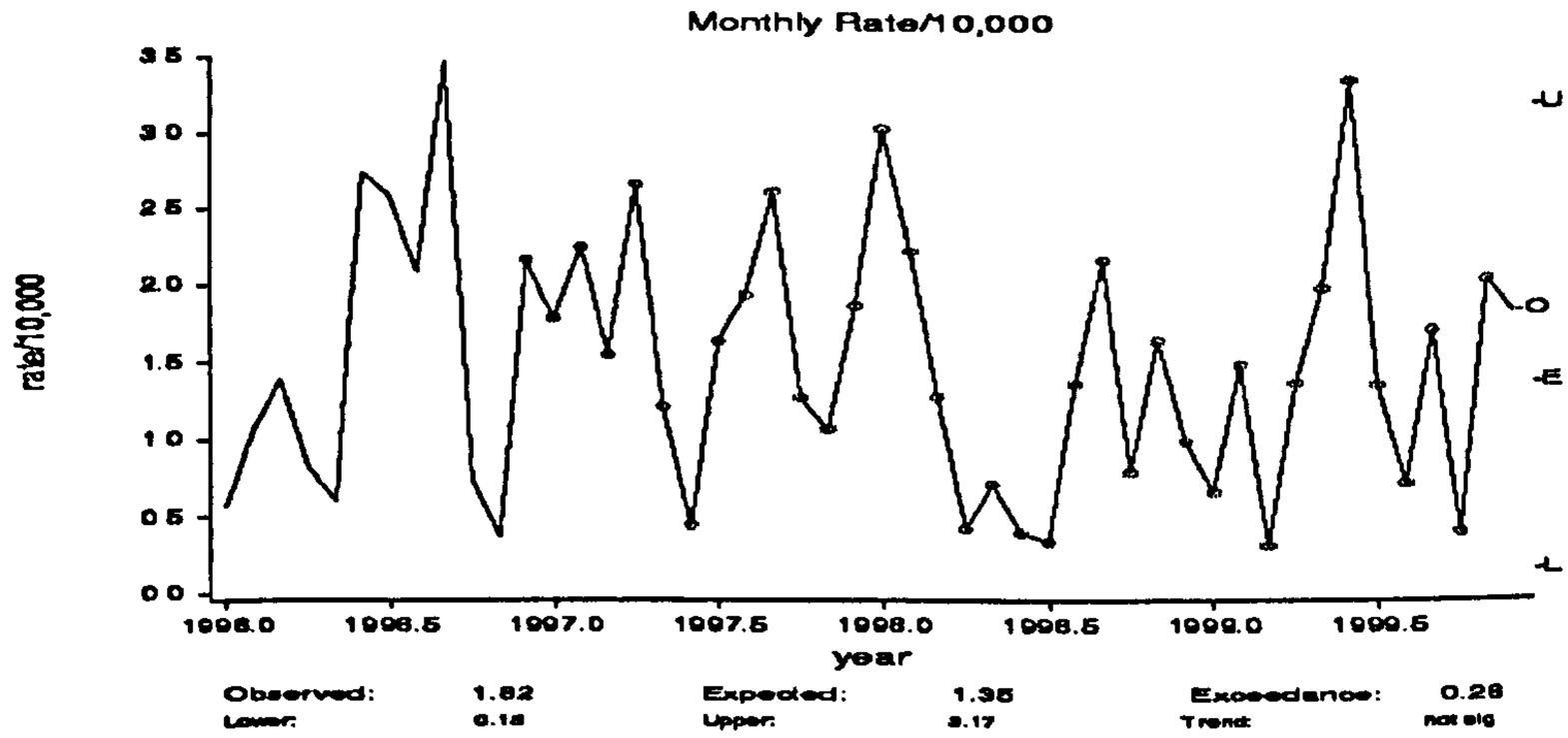
Old donor repeat reactors for T.pallidum antibodies



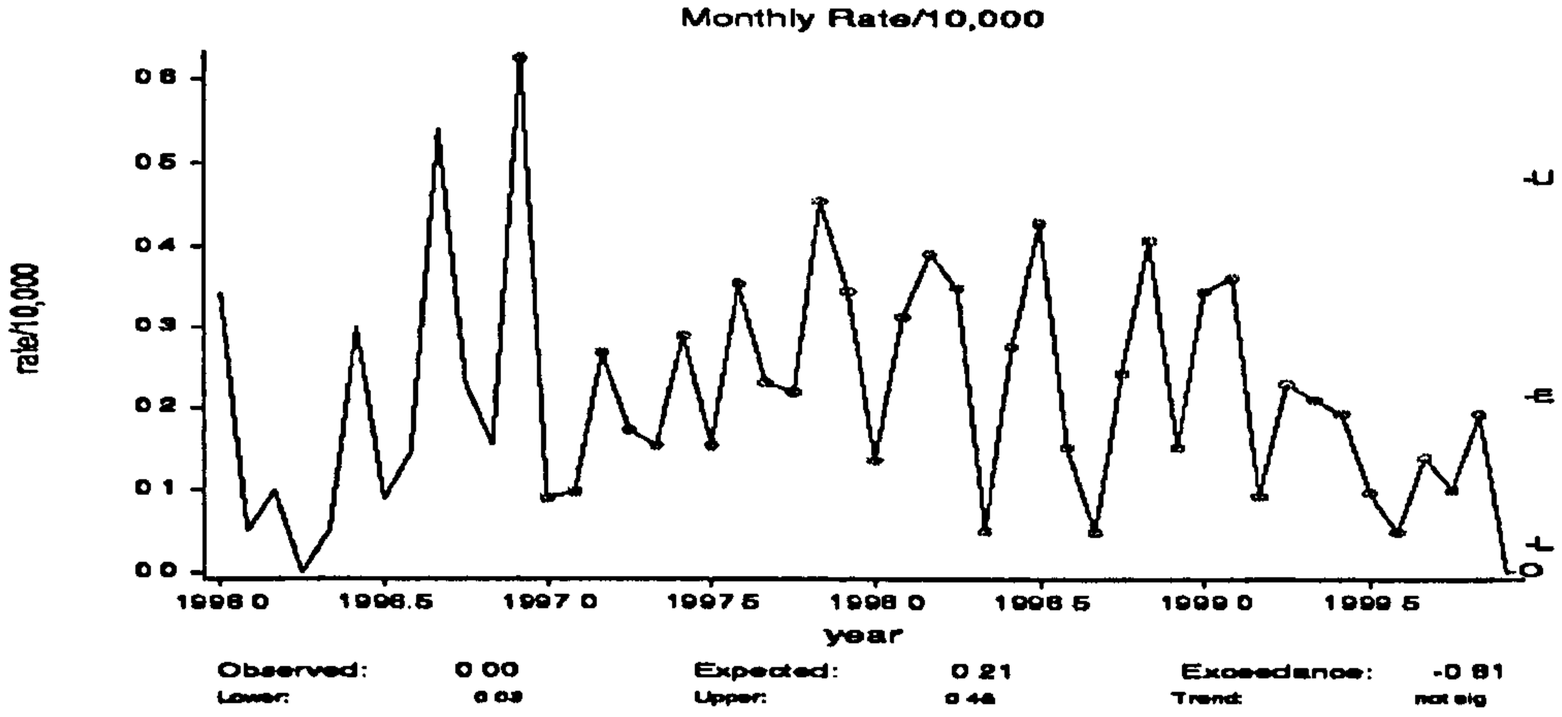
All donor repeat reactors for T.pallidum antibodies



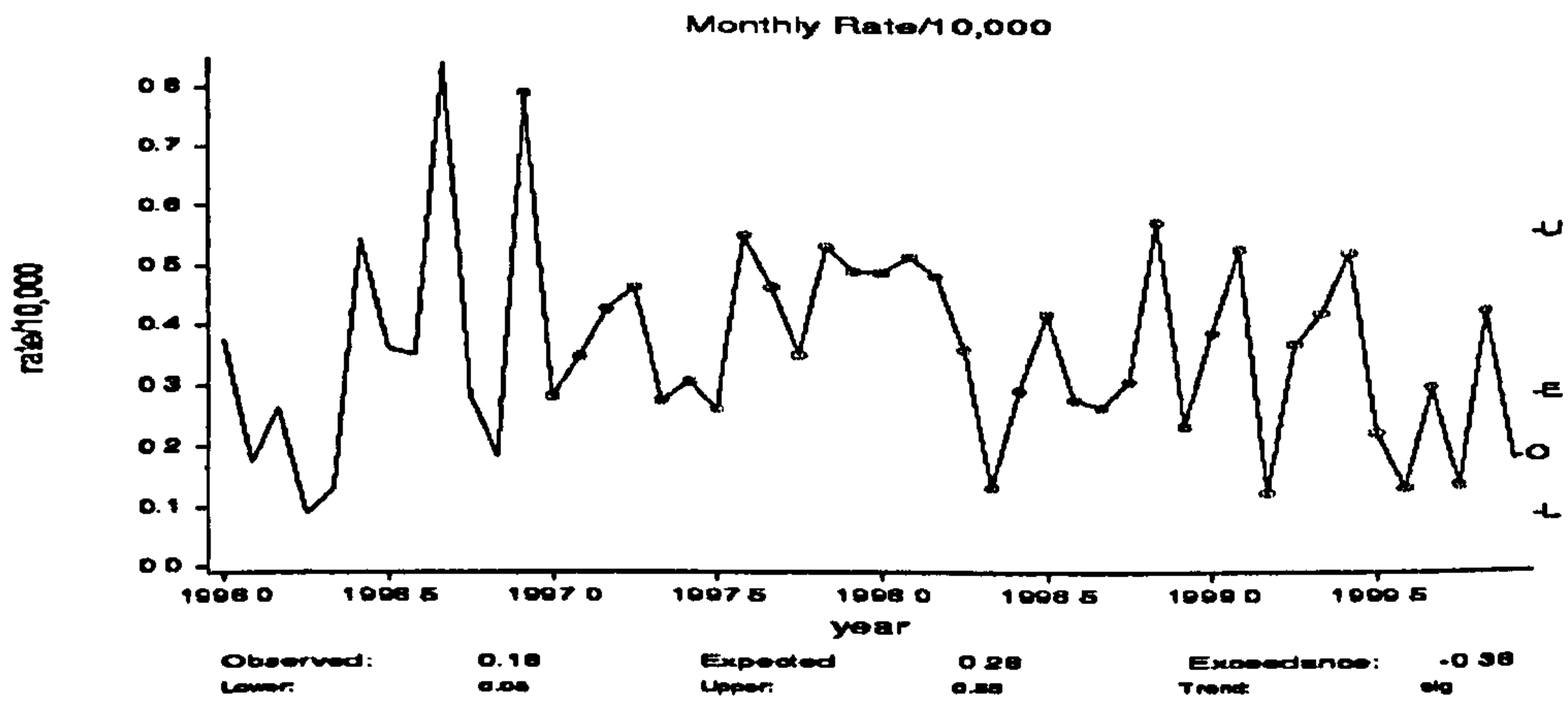
New donor Infections for T.pallidum antibodies



Old donor Infections for T.pallidum antibodies



All donor Infections for T.pallidum antibodies



Since September 1999 a statistical analysis has been run each month, using the reported data, to identify any unusual data that may indicate an important change in test performance, or in donor infection rates.

Analysis of Monthly donation testing data

During the first 12 months (September 1999 to August 2000), out of 288 observed repeatedly reactive rates and infected donor monthly rates this analysis identified (at the 5% significance level) 22 that were outside the 95% prediction intervals based on the previous 36 months observed data i.e. with an exceedance score greater or less than 1. These unexpected observed rates are shown in Table 3.4, with the exceedance score for the observed rate and the number of donations repeatedly reactive, or positive, that generated the observed rate.

Table 3.4 Unexpected repeatedly reactive (RR) rates and confirmed infection rates (at 5% significance level) observed in donation testing data for July 1999 - June 2000.

Month	Unexpected RR rate	Donor type	Exceedance score	Number RR
0100	HBsAg	New	1.40	55
0100	T.pall.	New	1.62	30
0200	anti-HCV	New	1.26	84
0200	anti-HIV	Repeat	-1.51	180
0200	anti-HIV	ALL	-1.26	230
0200	T.pall.	New	2.12	33
0200	T.pall.	ALL	1.08	190
0300	T.pall.	New	3.68	61
0500	T.pall.	New	1.83	42
0500	T.pall.	Repeat	1.43	246
0500	T.pall.	ALL	1.44	288
0899	T.pall.	ALL	-1.01	107
0999	T.pall.	Repeat	-1.08	80
0999	T.pall.	ALL	-1.02	98
1199	HBsAg	New	1.36	50
1299	HBsAg	New	-1.21	22
1299	anti-HCV	New	-1.19	61
1299	T.pall.	New	-1.21	13
18				

Unexpected infection rate	Donor type	Exceedance score	Number infected
HBsAg	Repeat	1.40	3
anti-HCV	Repeat	-1.24	1
anti-HIV	New	1.02	2
anti-HCV	ALL	1.12	24
4			

The majority (82%) of unexpected observations were repeatedly reactive rates: 61% of these (11) concerned repeat reactivity to test for Treponemal

antibodies. The repeatedly reactive rate for Treponemal antibodies in new donors was high for 4 months, and low for 1 month during this year. 44% of unexpected repeatedly reactive rates were unexpectedly low. Only 4 unexpected infection rates were observed at the 5% significance level, one was an unexpectedly low rate. Only one of the unexpectedly high infection rates was based on more than 5 infections. None of the unexpectedly high infection rates persisted for more than one month.

Analysis of monthly centre distribution of infected donors

One hundred and forty-one of 1,344 (10%) observed centre and donor type specific infection rates (i.e. proportion of donations tested found to be positive) during the first year (July 1999 to June 2000) were flagged as falling outside the probable range at the 5% significance level based on the previous 3 years' data. There was an average of twelve flagged centre and donor type specific infection rates per month (range 7 to 17 flagged values). An average of 6.8 flags each month (range 1 to 13) referred to rates based on more than two infections.

The average number of flags per month (and range) with various restrictions in place are shown in Table 3.5.

Table 3.5 Number (range) of flagged results per month meeting criteria, N = number of positive donations generating the rate, X^2 = value of chi-squared for the observed rate.

Possible criteria for further attention	***HBsAg***	***Anti-HCV***	***Anti-HIV***	***T.pall.***
All flagged rates	2.3 (0-3)	2.3 (1-4)	1.5 (0-3)	5.7 (0-11)
Flagged: N > 1	2.0 (1-3)	2.0 (1-3)	0.8 (0-2)	5.4 (0-10)
Flagged: N > 2	0.9 (0-1)	1.8 (0-3)	0	4.1 (0-9)
Flagged: N > 5	0.3 (0-1)	1.3 (0-3)	0	0.8 (0-4)
Flagged: X^2 > 5	2.3 (1-3)	2.3 (1-4)	1.5 (0-3)	5.7 (0-11)
Flagged: X^2 > 10	0.9 (0-2)	1.2 (0-2)	0	4.4 (0-8)
Flagged: N > 1 and X^2 > 5	2.0 (1-3)	2 (1-3)	0.8 (0-2)	5.4 (0-10)
Flagged: N > 3 and X^2 > 10	-	-	-	1.4 (0-5)

85 flags passed criteria of N >1 and X2 > 5 for HBsAg, anti-HCV and anti-HIV and N > 3 and X2 > 10 for T.pallidum: 9 of these flags appeared for one month only: the remainder appeared for at least 2 consecutive months. Twenty-five (29%) were on new donor infection rates and 60 (71%) were on repeat donor infection rates.

Infected donors

During the period of study, a total of 1,829 donations (16.83 per 100,000 donations) collected by the English and Welsh Blood services had markers of infectious HBV, HCV or HIV infection. Of these infected donations, 903 (49%) had anti-HCV, 463 (25%) had HBsAg, 94 (5%) had anti-HIV and 369 (20%) had Treponemal antibodies. New donors contributed 12% of all blood donations, but 70% of infected donations. Table 3.6 summarises the rate of infectious marker detection in donations from new donors, donations from repeat donors and in all donations, collected by the English and Welsh Blood Service during the period 01/10/95 to 30/09/99. The completeness of reporting to the infected donors surveillance was monitored by matching of reports for infected donors to confirmed positive donations reported to the donation testing surveillance. The completeness of reporting patient details, and of reporting follow-up clinical and risk factor details, is shown in Table 3.6 and Figure 3.5.

The distribution of infections by age group and by sex of donors is shown in Tables 3.7 and 3.8 and Figures 3.6 and 3.7 for newly tested donors and previously tested donors respectively.

Table 3.6 Infections detected in blood donors and the completeness of reporting: Donations collected in England and Wales from 01/10/1995 to 30/09/1999

Surveillance reports[1]	Infections in blood donors *Total*[4] 01/10/1995-30/09/1999			
	HBV (HBsAg)	HCV (anti-HCV)	HIV (anti-HIV)	*T.pallidum* (*Treponemal* antibodies)
a. Donations with confirmed marker of infection	463	903	94	369
- per 100,000 donations tested	4.26	8.31	0.86	3.39
- 1 in x donations	23,477	12,037	115,635	29,457
donations from new donors (1,207,079)	391	656	56	177
- per 100,000 donations tested	32.39	54.35	4.64	14.66
- 1 in x donations	3,087	1,840	21,555	6,820
donations from repeat donors[2] (9,662,571)	72	247	38	191
- per 100,000 donations tested	0.75	2.56	0.39	1.98
- 1 in x donations	134,202	39,120	254,278	50,589
b. Infected donors reported	463	873	94	358
- % of infections reported[3]	100%	97%	100%	97%
c. Exposure histories reported	358	702	78	252
- % of infections with exposure history reported[3]	77%	78%	83%	68%

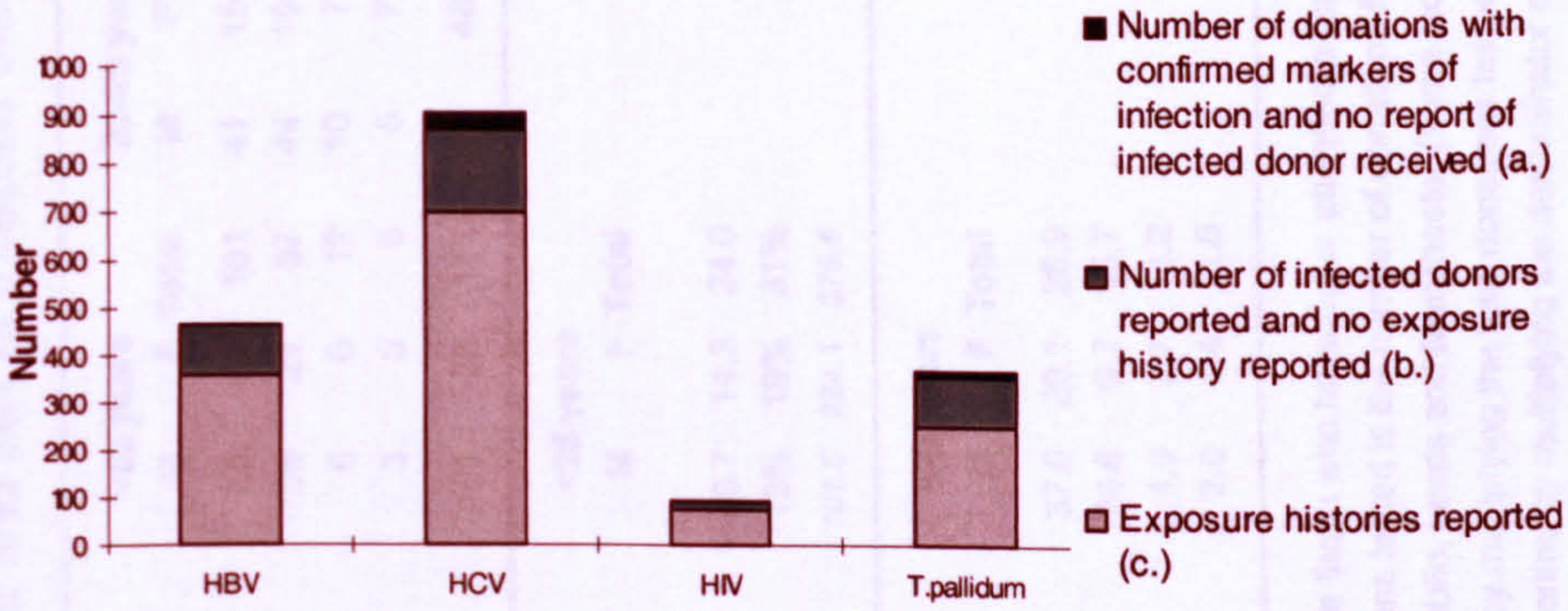
Source: a. Donation Testing Surveillance monthly reports, b. Infected Donor Surveillance Section 1 reports, c. Infected Donor Surveillance Section 2 reports.

[2] May include repeat donors newly tested for markers of infection.

[3] i.e. percentage of a.

[4] 9 donors had markers of more than 1 infection: 5 donors had HBsAg(carriage) and HCV, 1 donor had HBsAg(carriage) and HIV and 3 donors had HCV and Treponemal antibodies.

Figure 3.5. Infections detected in blood donors and completeness of reporting: Donations collected from 01/10/1995 to 30/09/1999



Descriptive epidemiology of infected donors

Table 3.7 Age and sex of infected blood donors: newly tested donors. Donations collected from 01/10/1995 to 30/09/1999

Reported infections	<25 years			25-29 years			30-34 years			35-39 years			40-44 years			45 years and over			Total			
	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	NK	Total
HBV(HBsAg)	56	45	101	41	15	56	37	11	48	41	19	60	34	14	48	49	36	85	258	140	3	401
HCV	36	21	57	44	19	63	102	61	163	128	59	187	100	72	172	80	44	124	490	276	2	768
HIV	6	6	12	10	7	17	10	4	14	4	3	7	2	0	2	1	2	3	33	22	0	55
T.pallidum	3	3	6	5	7	12	15	12	27	17	11	28	14	10	24	45	35	80	99	78	1	178
Total	101	75	176	100	48	148	164	88	252	190	92	282	150	96	246	175	117	292	880	516	6	1402

Donations tested[2] (thousands)	<25 years			25-34 years			35-44 years			45 years and over			Total		
	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total
By centres with known age & sex breakdown[3]	9.7	14.3	24.0	11.6	13.2	24.8	7.6	8.7	16.3	5.7	6.3	12.0	34.6	42.5	77.1
- % by age & sex	13%	19%	31%	15%	17%	32%	10%	11%	21%	7%	8%	16%	45%	55%	100%
All centres-*estimates*[4]	*151.5*	*224.1*	*375.6*	*181.2*	*206.9*	*388.1*	*119.5*	*136.5*	*255.9*	*89.0*	*98.4*	*187.4*	*541.2*	*665.9*	1207.1

Rate per 100,000 donations[5]	<25 years			25-34 years			35-44 years			45 years and over			Total		
	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total
HBV (HBsAg)	37.0	20.1	26.9	43.0	12.6	26.8	62.8	24.2	42.2	55.0	36.6	45.4	47.7	21.0	33.2
HCV	24.6	9.7	15.7	83.3	40.0	60.2	197.4	99.3	145.1	92.9	46.3	68.4	93.7	42.9	65.8
HIV	4.0	2.7	3.2	11.0	5.3	8.0	5.0	2.2	3.5	1.1	2.0	1.6	6.1	3.3	4.6
T.pallidum	2.0	1.4	1.6	11.4	9.5	10.4	26.7	15.9	20.9	52.1	36.7	44.0	18.9	12.1	15.2

[1] Infected donors include those who have never attended a reporting blood centre previously (i.e. "new" donors) and donors who have not been tested for the marker previously.

[2] The number of donations tested is the number of donations from "new" donors.

[3] Brentwood, Bristol, Dublin, Leeds and Manchester (some months).

[4] Estimates calculated by multiplying the total donations tested by the proportion found in each age and sex group at the four blood centres where age and sex breakdown was known

[5] Adjusted for underreporting by multiplying the denominator estimate for each age and sex group by the proportion of all detected infections reported (cf table 1).

Table 3.8 Age and sex of infected blood donors: previously tested donors. Donations collected from 01/10/1995 to 30/09/1999

Reported infections	<25 years			25-29 years			30-34 years			35-39 years			40-44 years			45 years and over			Total			
	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	NK	Total
HBV(HBsAg)	3	2	5	1	3	4	8	0	8	5	3	8	5	5	10	18	7	25	40	20	1	61
HCV	12	4	16	9	1	10	7	5	12	11	7	18	9	8	17	18	14	32	66	39	0	105
HIV	3	3	6	5	4	9	7	1	8	3	1	4	4	3	7	4	1	5	26	13	0	39
T.pallidum	2	1	3	4	3	7	7	7	14	6	6	12	18	10	28	74	39	113	111	66	3	180
Total	20	10	30	19	11	30	29	13	42	25	17	42	36	26	62	114	61	175	243	138	4	385

Donations tested[2] (thousands)	<25 years			25-34 years			35-44 years			45 years and over			Total		
	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total
By centres with known age & sex breakdown[3]	18.3	27.8	46.2	65.1	63.2	128.4	86.6	76.6	163.1	122.9	97.9	220.8	292.9	265.6	558.5
- % by age & sex	3%	5%	8%	12%	11%	23%	16%	14%	29%	22%	18%	40%	52%	48%	100%
All centres-*estimates*[4]	*317.1*	*481.4*	*798.5*	*1127.1*	*1094.2*	*2221.3*	*1497.8*	*1324.6*	*2822.4*	*2125.8*	*1694.6*	*3820.4*	*5067.8*	*4594.8*	9662.6

Rate per 100,000 donations[5]	<25 years			25-34 years			35-44 years			45 years and over			Total		
	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total
HBV (HBsAg)	0.9	0.4	0.6	0.8	0.3	0.5	0.7	0.6	0.6	0.8	0.4	0.7	0.8	0.4	0.6
HCV	3.9	0.9	2.1	1.5	0.6	1.0	1.4	1.2	1.3	0.9	0.9	0.9	1.3	0.9	1.1
HIV	0.9	0.6	0.8	1.1	0.5	0.8	0.5	0.3	0.4	0.2	0.1	0.1	0.5	0.3	0.4
T.pallidum	0.7	0.2	0.4	1.0	0.9	1.0	1.7	1.2	1.5	3.6	2.4	3.0	2.3	1.5	1.9

[1] Infected donors include only those "repeat" donors who have had a previous donation tested for the marker (but were not necessarily previously negative).

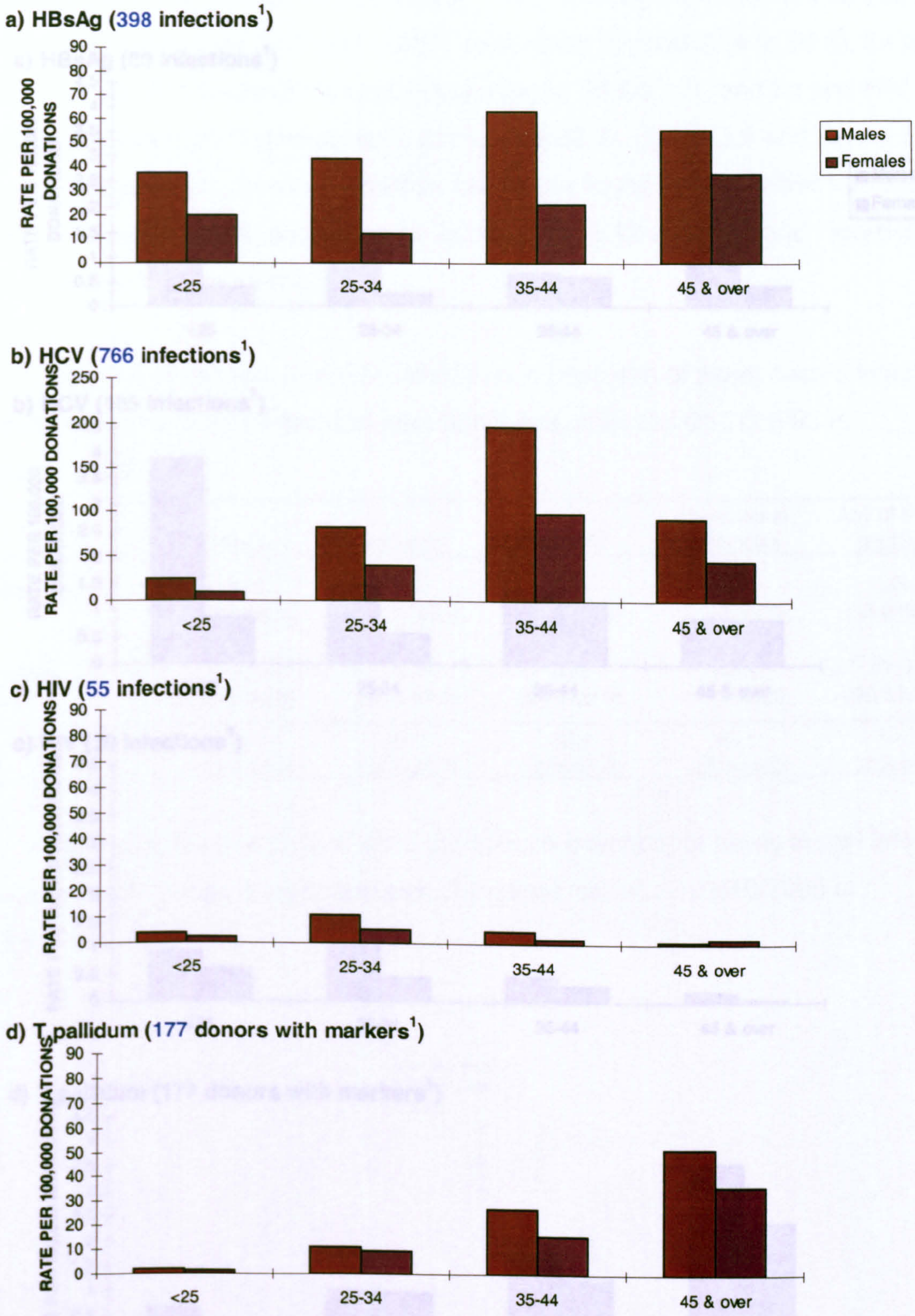
[2] The number of donations tested in the number of donations from "repeat" donors. Note - this will exceed the number of donors tested.

[3] Brentwood, Bristol, Dublin, Leeds and Manchester (some months).

[4] Estimates calculated by multiplying the total donations tested by the proportion found in each age and sex group at the four blood centres where age and sex breakdown was known.

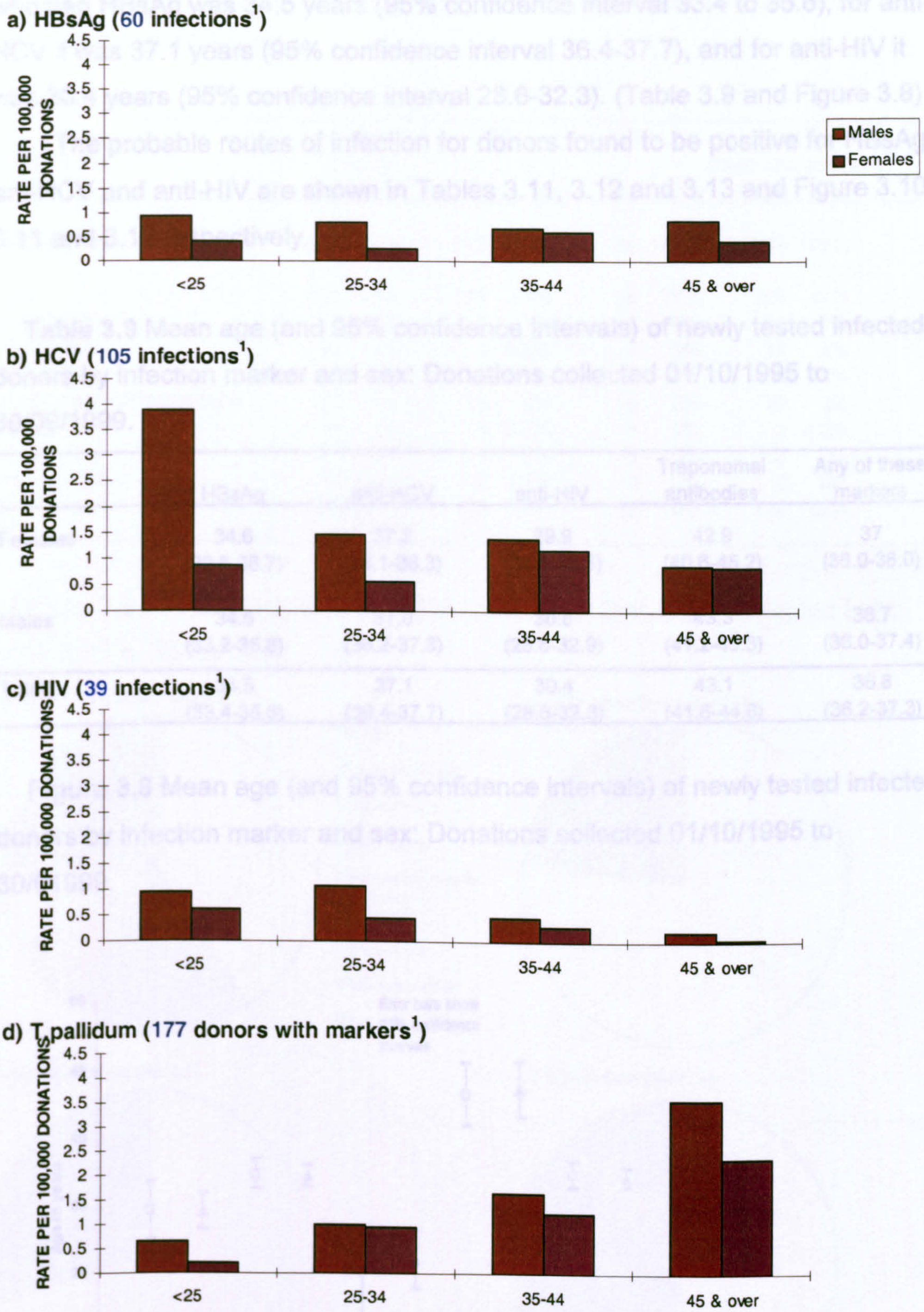
[5] Adjusted for underreporting by multiplying the denominator estimate for each age and sex group by the proportion of all detected infections reported (cf table 1).

Figure 3.6 Age and sex of infected blood donors: newly tested donors. Donations collected from 01/10/1995 to 30/09/1999.



[1] Rates adjusted for underreporting by multiplying the denominator estimate for each age and sex group by the proportion of all detected infections reported, e.g frequency of anti-HCV in males under 25 = (number anti-HCV positive males < 25 yrs /(number of donations, males < 25 yrs x 0.97[from table 3.6])).

Figure 3.7 Age and sex of infected blood donors: previously tested donors. Donations collected from 01/10/1995 to 30/09/1999.



[1] Rates adjusted for underreporting by multiplying the denominator estimate for each age and sex group by the proportion of all detected infections reported.

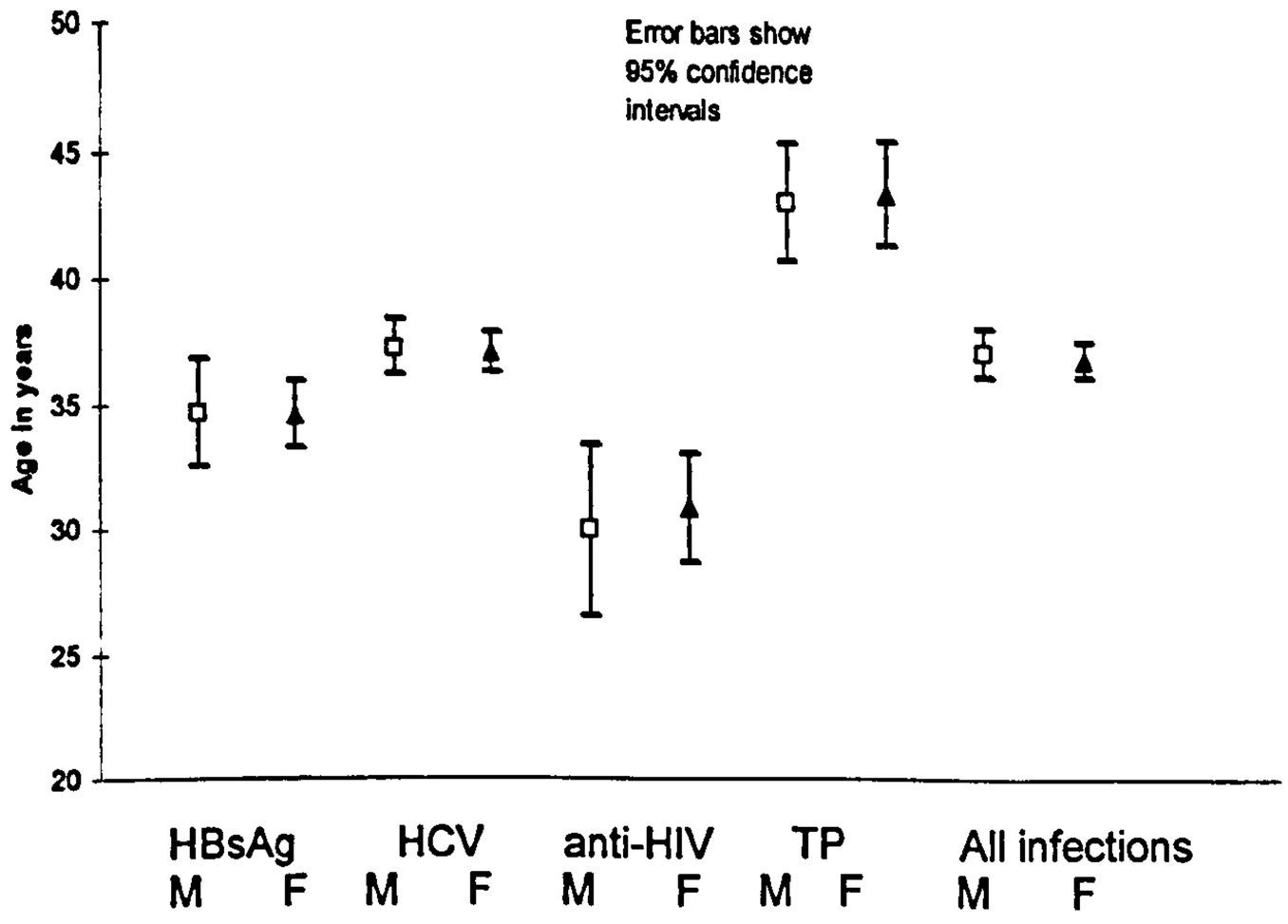
HBsAg and anti-HCV were 2.3 times and 2.2 times respectively more common in newly tested male donors than newly tested female donors. (chi-squared test $p<0.001$ for both markers). The mean age of newly tested donors who had HBsAg was 34.5 years (95% confidence interval 33.4 to 35.6), for anti-HCV it was 37.1 years (95% confidence interval 36.4-37.7), and for anti-HIV it was 30.4 years (95% confidence interval 28.6-32.3). (Table 3.9 and Figure 3.8)

The probable routes of infection for donors found to be positive for HBsAg, ant-HCV and anti-HIV are shown in Tables 3.11, 3.12 and 3.13 and Figure 3.10, 3.11 and 3.12 respectively.

Table 3.9 Mean age (and 95% confidence intervals) of newly tested infected donors by infection marker and sex: Donations collected 01/10/1995 to 30/09/1999.

	HBsAg	anti-HCV	anti-HIV	Treponemal antibodies	Any of these markers
Females	34.6 (32.5-36.7)	37.2 (36.1-38.3)	29.9 (26.5-33.3)	42.9 (40.6-45.2)	37 (36.0-38.0)
Males	34.5 (33.2-35.8)	37.0 (36.2-37.8)	30.8 (28.6-32.9)	43.3 (41.2-45.3)	36.7 (36.0-37.4)
Total	34.5 (33.4-35.6)	37.1 (36.4-37.7)	30.4 (28.6-32.3)	43.1 (41.6-44.6)	36.8 (36.2-37.3)

Figure 3.8 Mean age (and 95% confidence intervals) of newly tested infected donors by infection marker and sex: Donations collected 01/10/1995 to 30/01999.



The ethnic group of all donors was not available. The ethnic group of infected donors is shown in Table 3.10 and Figure 3.9.

Table 3.10 Ethnic group of infected blood donors. Donations collected from 01/10/1995 to 30/09/1999.

Ethnic group	HBV (HBsAg)		HCV		HIV		T. pallidum (Treponemal antibodies)	
	No.	%	No.	%	No.	%	No.	%
Infections reported	463	100%	873	100%	94	100%	358	100%
White	188	41%	671	77%	66	70%	169	47%
Black-Caribbean	12	3%	7	1%	8	9%	26	7%
Black-African	40	9%	4	0.5%	5	5%	14	4%
Black-Other	0	0%	0	0%	0	0%	3	1%
Indian/Pakistani/Bangladeshi	38	8%	15	2%	0	0%	10	3%
Chinese	34	7%	3	0.3%	0	0%	1	0.3%
Other Asian	40	9%	6	1%	0	0%	3	1%
Mixed and other	2	0.4%	2	0.2%	0	0%	0	0%
Not available	109	24%	165	19%	15	16%	132	37%

Figure 3.9 Ethnic group of infected blood donors. Donations collected from 01/10/1995 to 30/09/1999.

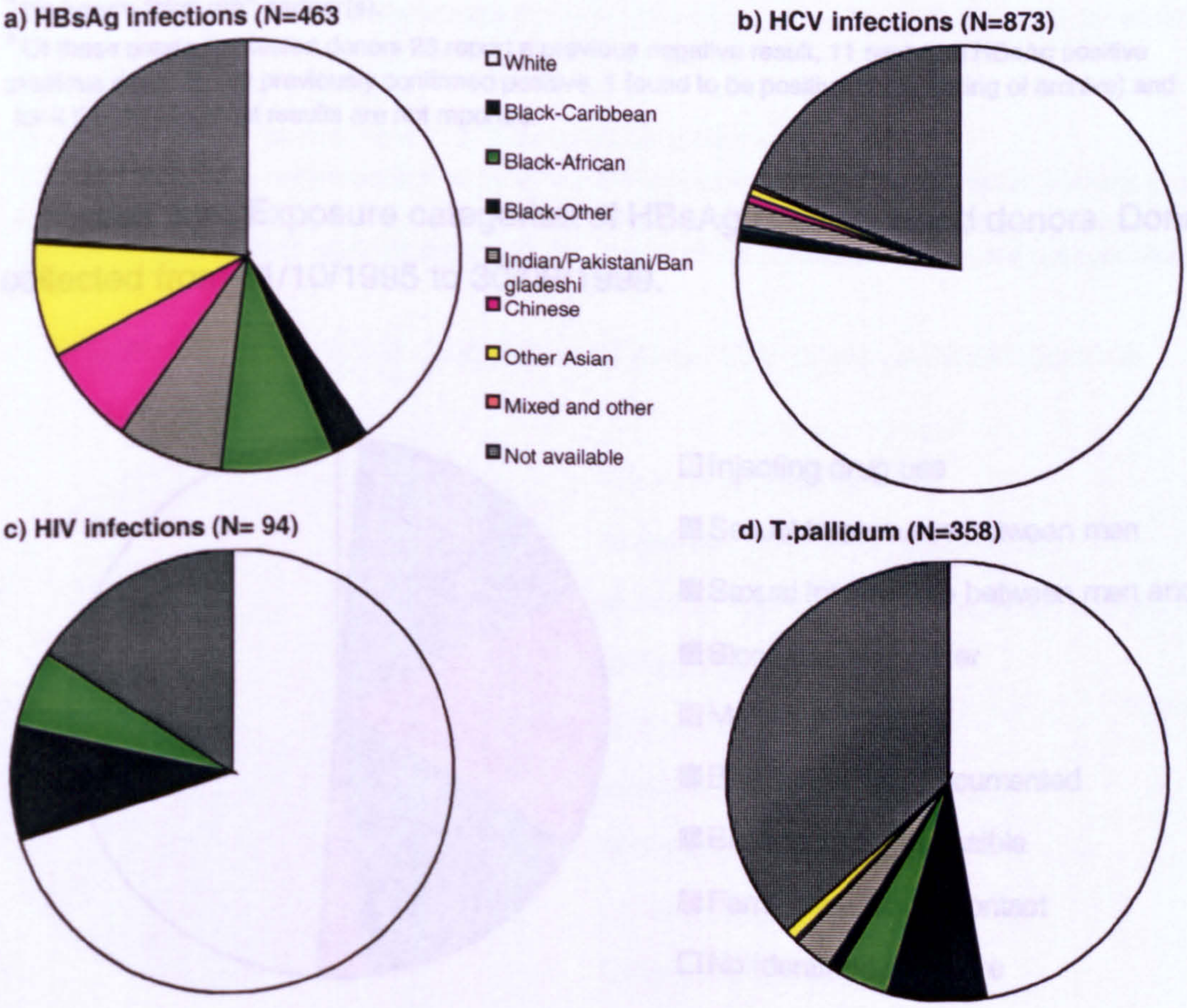


Table 3.11 Exposure categories of HBsAg positive blood donors. Donations collected from 01/10/1995 to 30/09/1999.

HBsAg positive blood donors How infection was probably acquired	Newly tested donors[1]	Previously tested donors	All donors HBsAg positive	%
Injecting drug use	4	1	5	1%
Sexual intercourse				
between men	3	0	3	1%
between men and women				
exposure to "high risk" partner(s)[2]	*4*	*1*	*5*	*1%*
exposure abroad[3]	*12*	*5*	*17*	*5%*
exposure in the UK[4]	*8*	*1*	*9*	*3%*
incomplete information	*9*	*3*	*12*	*3%*
Blood factor treatment	0	0	0	0%
Blood/tissue transfer	11	1	12	3%
Mother to infant	54	2	56	16%
Blood contact - documented	4	3	7	2%
Blood contact - possible	39	7	46	13%
Family/household contact	10	1	11	3%
No identified exposure	153	22	175	49%
Total	311	47 [5]	358	100%

[1] Newly tested by the blood transfusion services included in this surveillance: may have had donations tested in other countries.

[2] Partner(s) exposed through sexual intercourse with men, IDU, blood factor treatment or blood/tissue transfer.

[3] Individuals from abroad, and individuals from the UK who have lived or visited abroad, for whom there is no evidence of "high risk" partner(s).

[4] No known "high risk" partner(s).

[5] Of these previously tested donors 28 report a previous negative result, 11 report an HBsAg positive previous donation (10 previously confirmed positive, 1 found to be positive on re-testing of archive) and for 8 the previous test results are not reported.

Figure 3.10 Exposure categories of HBsAg positive blood donors. Donation collected from 01/10/1995 to 30/09/1999.

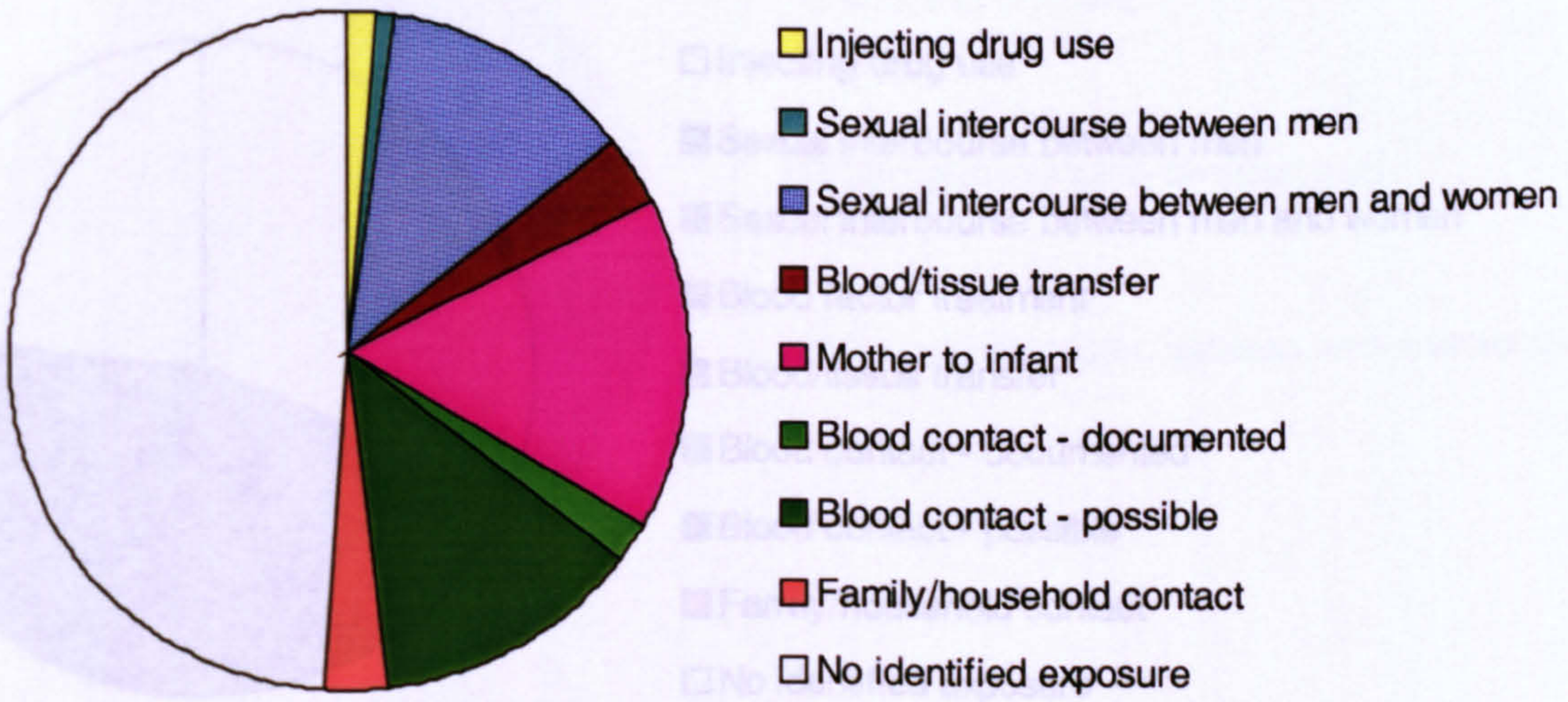


Table 3.12 Exposure categories of anti-HCV positive blood donors. Donations collected from 01/10/1995 to 30/09/1999.

How infection was probably acquired	Newly tested donors[1]	Previously tested donors	All donors HCV positive	%
Injecting drug use	209	9	218	31%
Sexual intercourse				
between men	0	1	1	0%
between men and women				
exposure to "high risk" partner(s)[2]	*49*	*3*	*52*	*7%*
exposure abroad[3]	*6*	*0*	*6*	*1%*
exposure in the UK[4]	*2*	*1*	*3*	*0%*
incomplete information	*1*	*1*	*2*	*0%*
Blood factor treatment	1	0	1	0%
Blood/tissue transfer	95	11	106	15%
Blood contact - documented	13	1	14	2%
Blood contact - possible[5]	120	17	137	20%
Family/household contact	2	1	3	0%
No identified exposure	132	27	159	23%
Total	630	72 [6]	702	100%

[1] Newly tested by the blood transfusion services included in this surveillance: may have had donations tested in other countries.

[2] Partner(s) exposed through IDU, blood factor treatment or blood/tissue transfer (pre Sept 91).

[3] Individuals from abroad, and individuals from the UK who have lived or visited abroad, for whom there is no evidence of "high risk" partner(s).

[4] No known "high risk" partner(s).

[5] Includes tattoos, acupuncture, possible occupational exposure to blood.

[6] Of these previously tested donors 35 report previous negative donations, 16 report previous reactivity not confirmed positive, 10 report previous positivity (8 previously confirmed positive, 2 found to be positive on re-testing of archive) and for 11 the results of the previous donation are not reported.

Figure 3.11 Exposure categories of anti-HCV positive blood donors.

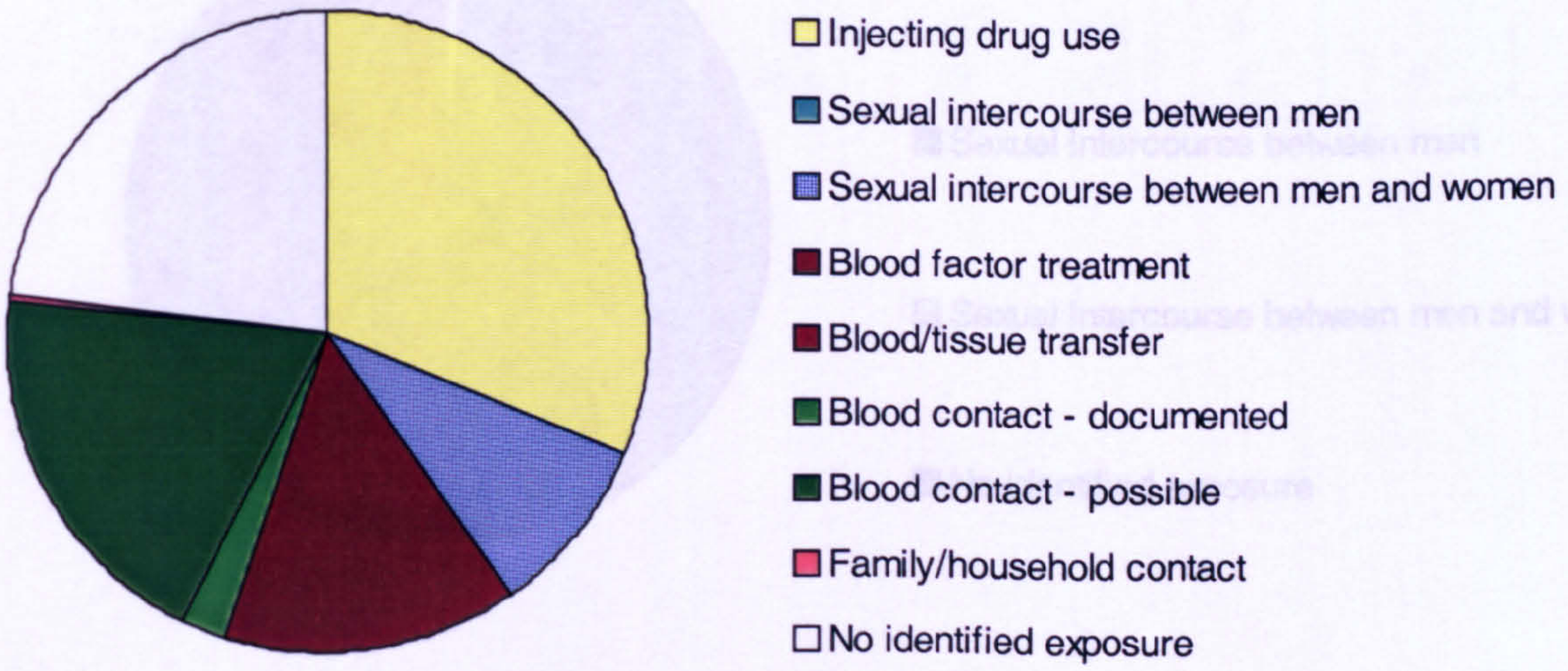


Table 3.13 Exposure categories of anti-HIV positive blood donors. Donations collected from 01/10/1995 to 30/09/1999.

How infection was probably acquired	Newly tested donors[1]	Previously tested donors	All donors HIV positive	%
Injecting drug use	1	0	1	1%
Sexual intercourse				
between men	13	16	29	31%
between men and women				
exposure to "high risk" partner(s)[2]	6	1	7	7%
exposure abroad[3]	8	7	15	16%
exposure in the UK[4]	11	11	22	23%
incomplete information	5	1	6	6%
Blood factor treatment	0	0	0	0%
Blood/tissue transfer	0	0	0	0%
Other	0	0	0	0%
No identified exposure[5]	11	3	14	15%
Total	55	39 [6]	94	100%

[1] Newly tested by the blood transfusion services included in this surveillance: may have had donation tested in other countries.

[2] Partner(s) exposed through sexual intercourse between men, IDU, blood factor treatment or blood/tissue transfer.

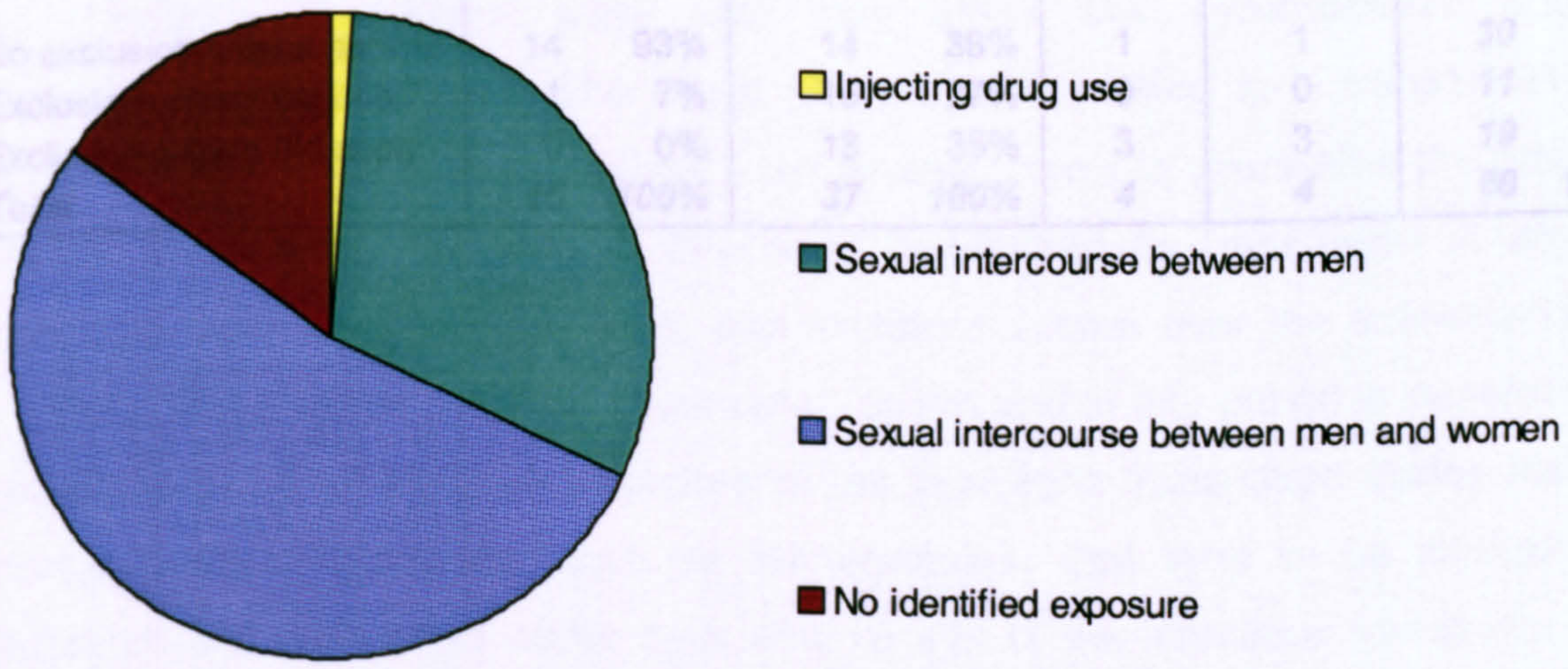
[3] Individuals from abroad, and individuals from the UK who have lived or visited abroad, for whom there is no evidence of "high risk" partner(s).

[4] No known "high risk" partner(s).

[5] Investigation continuing.

[6] All 39 positive previously tested donors had a previous anti-HIV tested donation in the UK recorded: all are reported to have been anti-HIV negative.

Figure 3.12 Exposure categories of anti-HIV positive blood donors. Donations collected from 01/10/1995 to 30/09/1999.



Exposure history information was reported for 67% of donors with confirmed reactivity for Treponemal antibodies: 27% of Treponemal antibody positive donors with exposure history information available had a history of Syphilis reported and 5% had a history of Yaws.

The second version of the infected donor surveillance form asked for reasons for non-disclosure prior to donation of probable routes of infection. 60 of 129 exposure histories reported on these new forms (to 30/06/1999) included a response to this question. The reasons donor selection criteria did not exclude these donors are shown in Table 3.14; amongst the remaining 59, only 2 reported an identified probable route of infection. For 30 of the 60, the probable route of infection was not a reason for pre-donation exclusion. For 11, the probable route of infection occurred outside the period of time for which the donor selection criteria apply. For 19 (13 HCV, 3 HIV and 3 TP) a risk factor was disclosed during post-diagnoses counselling that should have resulted in exclusion from donation: the reported reasons these risk factors were not disclosed prior to donation are shown in Table 3.15.

Table 3.14 Classification of applicability of donor selection criteria to infected donors with reasons why probable route of infection was not disclosed prior to donation reported (up to 30/06/1999).

	HBV	%	HCV	%	HIV	T. pallidum	*Total*	*%*
No exclusion criteria applied	14	93%	14	38%	1	1	*30*	*50%*
Exclusion criteria expired	1	7%	10	27%	0	0	*11*	*18%*
Exclusion criteria did apply	0	0%	13	35%	3	3	*19*	*32%*
Total	***15***	***100%***	***37***	***100%***	***4***	***4***	***60***	***100%***

Table 3.15 Reasons for non-disclosure prior to donation of risk factors for which exclusion criteria applied.

How infection was probably acquired	Infection	Reason stated for non-disclosure prior to donation
Injecting drug use	HCV	Single IDU only, therefore did not think it applied.
	"	Thought blood would be tested. Needed to know blood group for work.
	"	Told S.O. past history of hepatitis but informed by a hospital last year that no longer has it. Did not tick IDU because linked it with the hepatitis which had discussed with the S.O.
	"	Was only trying to help, and thought all was tested anyway.
	"	Did not think it relevant - a long time ago and did not share needles/syringes, although did share other injecting equipment[1]
	"	Did not think it was relevant as it was along time ago.
	"	Thought it was too long ago to matter.
	"	Knows others in the same situation who are long-term donors.
	"	Did not fully understand the safety of blood leaflet.
	"	Asked for advice prior to session, and was assured that if had been cleared of hepatitis B and it was more than 12 months ago, it was OK.
	"	Didn't adequately read safety of blood leaflet. Also tries to forget one episode of IDU.
Sexual intercourse between men	HIV	Says that discussed with GP who told him it was OK to donate, and thinks "Blood Service has a prejudice against gays"[2]
	"	Did not see risk as had not had anal sex, and rated oral sex as messing around only.
	"	Regular donor - hard to self-exclude now.[3]
	T.pallidum	Assumed infection fully eradicated therefore OK.[4]
Sexual intercourse between men and Women	HCV	Thought was in the clear as partner said had never shared a needle - only spoons (heroin addict) and was tested and negative in the past.
	"	Did not understand that spouse's history excluded donor, as spouse in no longer using drugs.
	T.pallidum	Has had blood tests before but no positive results.
	"	Not aware of risk.

Notes: 1,2,3&4 were repeat donors. 1= not previously tested. 2,3 = previously negative. 4 = previously reactive.

Transfusion-transmitted infections

Infectious complications following transfusion differ from non-infectious complications in several ways that may affect the ascertainment and investigation of incidents. The onset of symptoms related to a transfusion-transmitted viral infection may occur from several weeks to years after the date of the transfusion. Reports of infections transmitted by transfusion in any particular year, or period of years, can therefore accrue over the subsequent year(s). The number of cases ascertained by the end of any period is therefore expected to be an incomplete picture of the infections transmitted during that period. Acute infections, such as bacteraemias, that tend to be clinically apparent and diagnosed within days after receipt of the infectious transfusion, may be relatively complete but chronic viral infections will be underrepresented.

In addition, the occurrence of disease, or the observation of serological markers of infection, in individuals who have donated blood can lead to the ascertainment of transfusion-transmitted infections by tracing and testing of recipients exposed to components collected from donors during potentially infectious periods. Recipients may be asymptomatic at this time and only identified by this investigation.

Post-transfusion infections (PTI) may be due to an infected (or contaminated) transfusion or infection may have been acquired from another source. Investigation of markers of infection in an implicated donation, or in subsequent samples from the donors of implicated donations, can confirm transfusion as the probable cause of infection, or identify the need to investigate other possible sources. The blood service must therefore be informed about implicated transfusions so that investigations can be conducted to confirm or refute the suspicion that the implicated transfusion(s) may have been infectious. This is essential to prevent further transmission(s) by other components and/or by chronically infected donors, and to reveal any systematic errors or deficiencies in the blood service testing. Such investigations may involve microbiological testing of many donors and may take several months to complete.

One category of post-transfusion infections is not included in these data. In January 1999, a meeting of reporters agreed that HCV and HIV infections diagnosed in recipients who had received transfusions in the UK that were not tested for anti-HCV (i.e. pre September 1991) or anti-HIV (i.e. pre October 1985) respectively should be excluded from reporting. The blood service is rarely able to conduct follow-up investigation of donors implicated in these cases and these cases do not contribute to knowledge of the current infection transmission risks of blood transfusions. Numbers and details of such infections were therefore not included in data for the surveillance system after January 1999, and 4 previous reports have been excluded retrospectively.

Data received by 31/12/99 about incidents of transfusion-transmitted infections initially reported by blood centres during the four years from 1/10/95 to 30/9/99 are included in this thesis.

Unless the investigation was closed due to the identification of a probable source of infection other than transfusion, investigations that were closed without being able to conclusively investigate the source of the post-transfusion infections were classified as post-transfusion infections with inconclusive investigation. Table PTI 1 and Figure PTI 1 show the number of reports by their status by report year.

Table PTI 1 Status of post-transfusion infections reported 01/10/1995 to 30/09/1999 by report year.

Report year	Outcome of donor investigation/comment				
	Probable transfusion transmitted infection	Investigation concluded not transfusion-transmitted	Inconclusive investigation	Full investigation pending	*Total* [1]
1. 01/10/95-30/09/96	3	8	1	0	*12*
2. 01/10/96-30/09/97	8	12	4	3	*27*
3. 01/10/97-30/09/98	3	20	8	2	*33*
4. 01/10/98-30/09/99	7	17	3	8	*35*
Total	*21 (19%)*	*58 (54%)*	*16 (15%)*	*13 (12%)*	*108*

[1] An additional 23 post-tranfusion reactions suspected to be due to bacteria were reported.

Figure TTI 1. Post-transfusion infection (PTI) reports by report year.

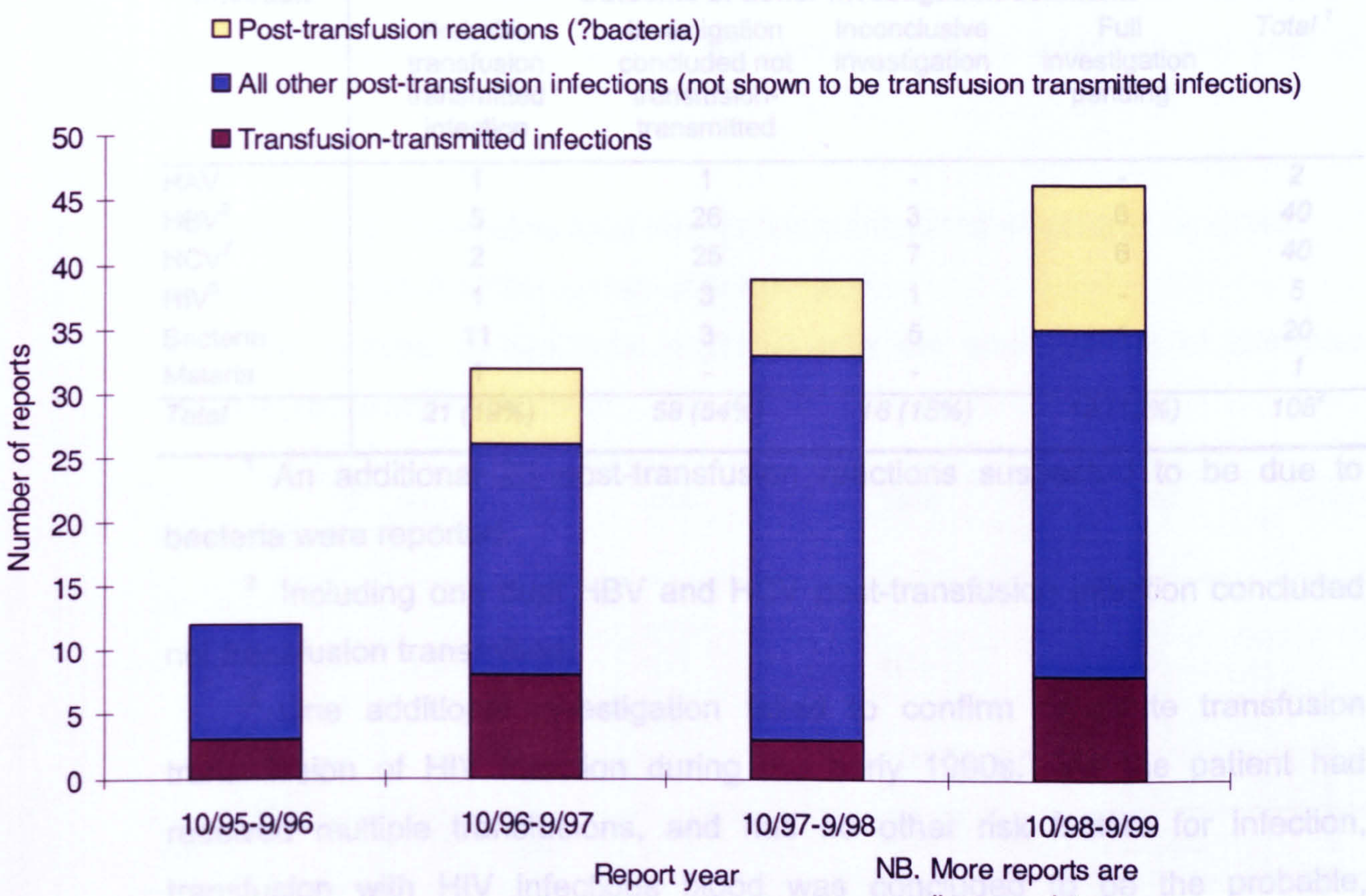


Table PTI 2 shows the number of reports by their status and by infection. Figure PTI 2 shows the status of reports up to the end of September 1999 at 31/12/99.

Table PTI 2 Status of post-transfusion infections reported 01/10/1995 to 30/09/1999 by infection.

Infection	Outcome of donor investigation/comment				
	Probable transfusion transmitted infection	Investigation concluded not transfusion-transmitted	Inconclusive investigation	Full investigation pending	*Total* [1]
HAV	1	1	-	-	*2*
HBV[2]	5	26	3	6	*40*
HCV[2]	2	25	7	6	*40*
HIV[3]	1	3	1	-	*5*
Bacteria	11	3	5	1	*20*
Malaria	1	-	-	-	*1*
Total	*21 (19%)*	*58 (54%)*	*16 (15%)*	*13 (12%)*	*108*[2]

[1] An additional 23 post-transfusion reactions suspected to be due to bacteria were reported.

[2] Including one dual HBV and HCV post-transfusion infection concluded not transfusion transmitted.

[3] One additional investigation failed to confirm or refute transfusion transmission of HIV infection during the early 1990s. As the patient had received multiple transfusions, and had no other risk factors for infection, transfusion with HIV infectious blood was concluded to be the probable, although unproven, source of infection.

Figure PTI 2 Post-transfusion infections reported 01/10/1995 to 30/09/1999.

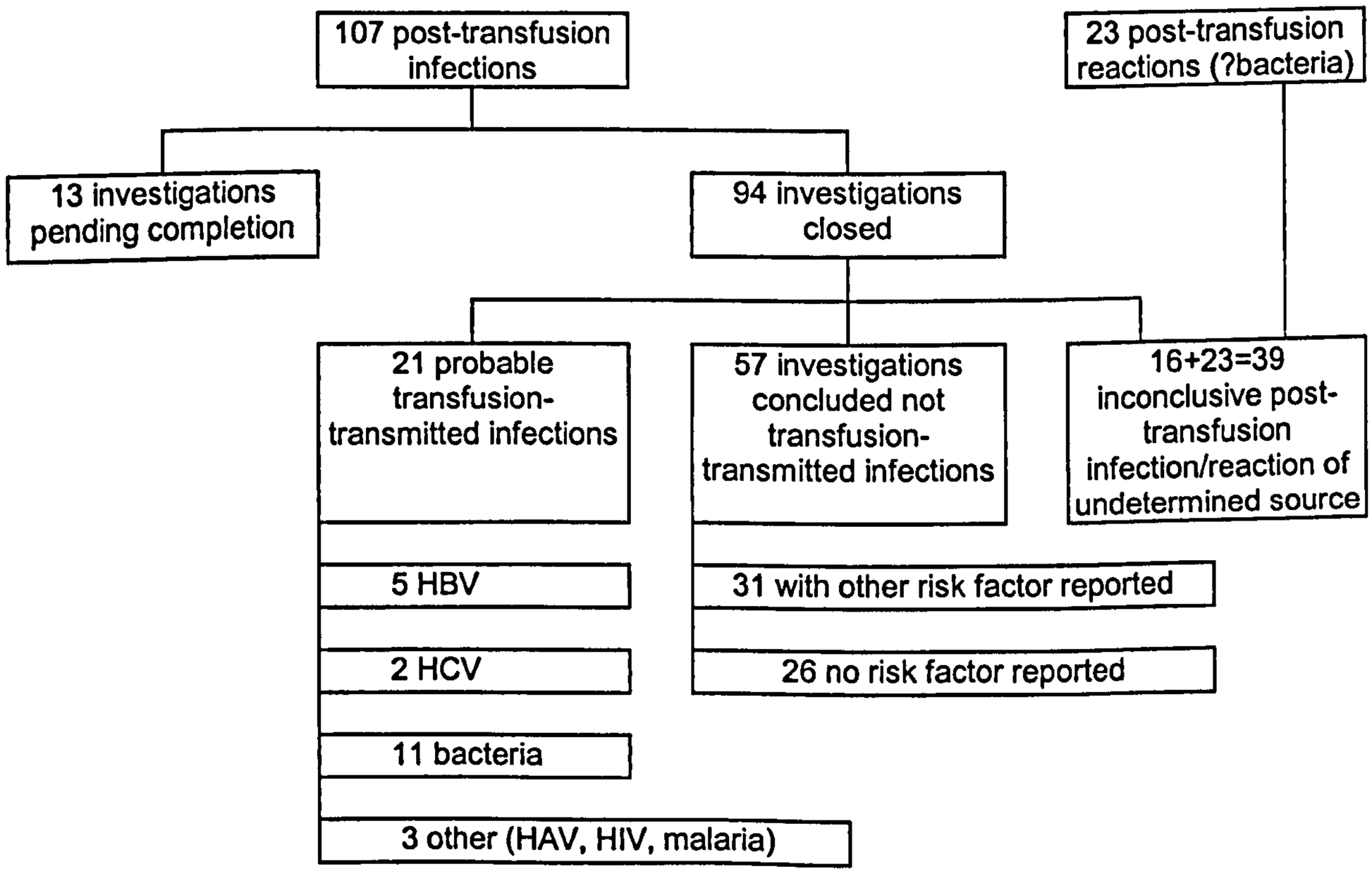


Table PTI 3 shows the cumulative number of transfusion-transmitted infections reported by the end of September 1999 by infection and year of transfusion.

Table PTI 3 Cumulative total transfusion-transmitted infections: reported between 1/10/95-30/9/99 by date of transfusion.

The number of incidents is shown with the total number of identified infected recipients in brackets.

Year of transfusion	pre-1995	1995	1996	1997	1998	1999 (to end Sept)	Total	Deaths
Infection								
HAV	-	-	1(1)	-	-	-	1(1)	
HBV	1(1)[b]	1(1)	1(1)	1(1)	1(1)-		5(5)	
HCV	-	-	1(1)	1(1)	-		2(2)	
HIV[c]	-	-	1(3)	-	-	-	1(3)	
Bacteria	-	1(1)	1(1)	3(3)	3(3)[ax2]	3(3)[a]	11(11)	3
Malaria	-	-	-	1(1)[a]	-	-	1(1)	1
Total	1(1)[b]	2(2)	5(7)	6(6)[a]	4(4)[ax2]	3(3)[a]	21(23)	4

Notes: [a] Infection was implicated in the death of a recipient.

[b] One household member who was caring for the recipient has been diagnosed with acute HBV.

[c] One additional investigation, initially reported during 97-98 and concluded during 98-99, failed to confirm or refute transfusion transmission of HIV infection during the early 1990s. As the patient had received multiple transfusions, and had no other risk factors for infection, transfusion with HIV infectious blood was concluded to be the probable, although unproven, source of infection.

During the first four years of reporting (i.e. 01/10/95 to 30/09/99) to the surveillance system for post-transfusion infections, 107 post-transfusion infections were reported (including 1 dual infection). Twenty-one were classified, after investigation, as transfusion transmitted infections (see Table PTI 3). Sixteen (15%) post-transfusion infections were classified as post-transfusion infections of undetermined source due to incomplete investigation of the transfusion(s) implicated as the source of the infection. For 58 (54%) post-

transfusion infection reports, investigation into the case was completed and no evidence was found to implicate transfusion as the source of infection. At least one other risk factor for infection other than transfusion was identified for 31 (53%) of these infections.

During the years 1996-1999 an additional 23 reports were received about post-transfusion reactions that were suspected to be due to bacteria but for which no evidence of bacterial infection (or endotoxin) that could have caused the reaction was sought and found in the recipient or implicated component (i.e. did not satisfy the criteria for a post-transfusion infection as stated above, but may have been reactions of bacterial origin). These reports started during the second report year when a parallel system for reporting non-infectious hazards of transfusion was established and hospitals were encouraged to report all post-transfusion complications. A new category was added to the report form for these cases as they were clinically important post-transfusion complications. The absence of confirmation of infection in the recipient was likely - at least in some cases - to be due to absence of the appropriate sample for testing, rather than absence of any infection. The cause and source of these cases cannot be resolved as certainly as the other cases, and they are presented separately throughout.

Reports were received from 15 of the 21 blood centres (between 1-16 cases each) participating in the surveillance system. The six centres that did not report any cases included 3 small centres that tested less than five thousand donations per year. These six centres collect approximately 5.4% of the donations tested by blood centres participating in the surveillance system. Seven hospital clinicians reported more than one infection: 23 hospitals transfused more than one of the investigated recipients (20 x 2 reports, 2 x 3 reports, 1 x 4 reports).

Post-transfusion reactions:

None of the 23 post-transfusion reactions suspected to be due to bacteria were clearly shown to be due to transfusion-transmitted bacteria. Six of these recipients died: for one the transfusion reaction was implicated in the death of the recipient. Brief details of these cases are shown in table PTI 4.

Table PTI 4 Cases of post-transfusion reactions suspected to be due to bacteria.

Report year	PTR organism	PTR symptoms	PTR organism in unit	PTR organism in recipient	PTR other source
2		Febrile, back pain	No	No	
2		Unspecified reaction	No	No	
2	Staph. warneri	Pyrexia, breathless, hypertension	Yes (contamination?)	No	
2		Febrile, hypertension	No	No	
2	Pseudomonas aeruginosa	Cardiovascular collapse, respiratory arrest	Yes (contamination?)	No	
2		Hypertension	No	No	
3	Pseudomonas vesicularis	Febrile	Yes (contamination?)	No	
3		Hypotension, trachycardia	No	No	
3	Mixed	Hypotension, breathless, died(cardiac arrest)	Yes (contamination?)	No	
3	Serratia liquifacians	Febrile, rigors	Yes	No	
3	E.coli	Hypotension, faint, cyanosis	Yes	No	
3	Staph. epidermidis	Unspecified reaction	Yes (contamination?)	No	
4		Allergic reaction, wheezing, hypoxia, uticarial rash	No	No	?HLA
4		Rigors, (died-aortic aneurysm)	No	No	
4		Died(cardiac arrest)	No	No	
4		Unspecified reaction	No	No	
4		Febrile, rash	No	No	
4		Unspecified reaction, died(other causes)	No	No	
4		Hypertension, pulmonary oedema	No	No	
4		Hypotension, rash, pulmonary oedema	No	No	?Trali
4		Unspecified reaction	No	No	
4		Septicaemia reaction	No	No	
4		Unspecified reaction, died(other causes)	No	No	

Details of transfusion transmitted infections

A. Infections for which donation testing is mandatory

Hepatitis B virus

Five transfusion transmitted HBV infections were reported.

HBV1. One recipient (29 year old female) had clinical acute HBV infection four months after transfusion of 2 red cell units. One donor was found to have a history of HBV infection 5 years prior to the implicated donation and to be anti-HBc positive and anti-HBs negative (HBV DNA negative). An HBV infectious, HBsAg negative, donation collected from a donor during the tail end of carriage of HBV infection was concluded to be the probable source of the recipient's HBV infection.

HBV2. One recipient (26 year old male) had acute clinical HBV infection five months after transfusion of a red cell unit (one of 14 red cell units given over a year) that was found, by testing of the archived sample of the donation to be anti-HBc negative but HBV DNA positive. At the time of the investigation, the donor recalled having viral symptoms and abdominal pains 5 months post-donation and was found to be anti-HBs positive. The probable source of the recipient's HBV infection was concluded to be an HBV infectious though HBsAg negative and anti-HBc negative donation collected from a repeat donor during early acute infection.

HBV3. One recipient (67 year old female) had acute HBV infection five months after transfusion of three red cell units. One of the donors was found to have markers of resolved HBV infection eleven months after donating the implicated donation. An HBV infectious, HBsAg negative, donation collected from a donor during acute (asymptomatic) infection was concluded to be the probable source of the recipients HBV infection.

HBV4. One recipient (59 year old male) was found to be an HBsAg and HBeAg positive HBV carrier 6 years after transfusion with 8 red cell units. One of the donors was found to have markers of resolved HBV infection and it was also discovered that this donor had developed acute HBV (confirmed by the local laboratory) 3 months after donating the implicated donation. No archived sample of the donation was available for further testing. The probable source of the recipient's HBV infection was concluded to be an HBV infectious but HBsAg negative donation collected from a new donor during acute infection. Secondary transmission seems to have occurred as a household member who was caring for the infected recipient was diagnosed with acute HBV at the same time as the recipient's diagnosis.

HBV5. One recipient (73 year old female) was found to have markers of acute HBV infection four months after transfusion of a red cell unit (one of three units received during a month) collected from a donor who developed acute HBV infection between one and two months after donating blood. The recipient was traced after the donor's General Practitioner informed the blood service of the donor's infection status. The archive of the implicated donation was confirmed to be HBsAg negative on re-testing but was found to be HBV DNA positive by nested PCR. (DNA was not detectable by PCR on a 1 in 96 dilution.) The recipient died three months after her HBV diagnosis from the

underlying reason for transfusion: HBV infection was not implicated in the recipient's death. The probable source of the recipient's HBV infection was concluded to be an HBV infectious, though HBsAg negative, donation collected from a repeat donor during early acute infection. The blood donor did not report any risk factor for HBV infection that is currently included as criteria for the exclusion of individuals from donating blood.

Both of the donations implicated in cases HBV3 and HBV4 above were collected from donors who subsequently disclosed risk factors for HBV infection that should, according to donor selection criteria in place at the time, have been recognised as making them ineligible for blood donation. Further investigation is needed to identify the reasons why these donors were not recognised as ineligible for donation.

Hepatitis C virus

Two transfusion transmitted HCV infections were reported.

HCV1. One recipient (79 year old female) was traced and tested for HCV infection, seven months after transfusion with a single red cell unit, when a repeat donor was shown to have seroconverted for anti-HCV between donations. The pre-seroconversion donation was subsequently shown by testing of the archived sample to be HCV RNA positive. An HCV infectious, anti-HCV negative, donation collected from a repeat donor during acute (asymptomatic) infection was concluded to be the probable source of HCV infection for the recipient.

HCV2. A repeat donor was found to be anti-HCV positive and HCV RNA positive. The archived sample of the previous (first) donation from this donor was re-tested and was also anti-HCV and HCV RNA positive. The recipient (a 64 year old male) of this red cell unit was traced and tested fourteen months after transfusion and was found to be anti-HCV positive and HCV RNA positive. Investigation by the blood service found an error had occurred during the re-testing of the donation that was initially reactive to the anti-HCV test. The duplicate repeat tests were read as negative because the samples were unintentionally dispensed into blank wells that are used to fill out part plates so they can be handled by automated machinery. It had been common practice to blank these out with a black marker pen so that in the event they were accidentally used for samples they would return a fail-safe positive reaction.

However new machinery had been introduced which read these as negative. Once the problem was identified corrective and preventative action was put in place to ensure that a different mechanism is used to ensure that blank wells will, if accidentally used, return a positive result and "fail safe". The probable source of the recipient's HCV infection was concluded to be an HCV infectious, anti-HCV positive, donation from a new donor. The donation was not excluded from the blood supply because of a laboratory error during the testing process.

The donations implicated in cases HCV1 and HCV2 were collected from donors who did not report any risk factor for HCV infection that are currently included as criteria for the exclusion of individuals from donating blood.

HIV

One transfusion transmitted HIV infection was reported.

HIV1. A recipient (47 year old female) was tested for HIV infection when she developed signs of HIV infection, after transfusion therapy involving over 100 units of red cells and platelets over a seven-month period. The archived sample of one donation (giving rise to a platelet unit transfused to the patient), from a repeat donor who had not been shown to be anti-HIV negative on a subsequent donation, was found to be HIV DNA positive. The donor was subsequently found to be anti-HIV positive. An HIV infectious, anti-HIV negative, donation collected from a repeat donor during acute (asymptomatic) infection was concluded to be the probable source of the recipients HIV infection[1]. The recipients of the red cells and the fresh frozen plasma produced from the infectious donation were subsequently shown to have also been infected with HIV by transfusion (one recipient had died of non-HIV-related causes).

The donation implicated in case HIV1 was collected from a donor who subsequently disclosed risk factors for HIV infection that, according to donor selection criteria in place at the time, made the donor ineligible to donate blood.

B. Infections for which donation testing is not mandatory

Bacteria

Eleven transfusion-transmitted bacteraemias were reported.

BAC1. One recipient (male, age not reported) suffered septic shock after transfusion with 2 platelet units. The same serotype of group B streptococcus was isolated from the patient, the implicated unit and from a throat swab from the donor.

BAC2. One recipient (21 year old female) developed rigors, nausea, and peripheral vasoconstriction soon after transfusion with a pooled platelet unit began. *B. cereus* serovar H18 was isolated from the platelet pool and from the arm of one of the donors who contributed to the pool.

BAC3. One recipient (21 year old female) entered endotoxic shock after transfusion with a red cell unit. The red cell unit was subsequently found to be haemolysed and was shown to contain *Serratia liqufaciens*. No evidence of infection was found in the donor by arm swabbing and by testing blood for antibodies. The source of the contamination was not identified.

BAC4. One recipient (4 year old male) suffered a bacteraemia after transfusion with a platelet unit. *Escherichia coli* was cultured from the pack and from the patient. No damage to the pack or source of the contamination was identified.

BAC5. One recipient (61 year old female) suffered a bacteraemia after transfusion with a (leucodepleted) pooled platelet unit. The pack and an arm swab from one of the four donors were both shown to contain *Bacillus cereus*, serotype H29.

BAC6. One recipient (32 year old female) developed a bacteraemia after transfusion with red cells and platelets and died two days after the transfusion. *Staphylococcus aureus* was isolated from the recipient and from skin and nasal swabs from one of the implicated donors.

BAC7. One recipient (27 year old male) developed bacteraemia after transfusion with two leucodepleted, 4-day-old apheresis platelet units from the same donor. The recipient recovered and was asymptomatic one week after the transfusion. *Staphylococcus epidermidis* was isolated from the platelet packs and from the recipient (and these two isolates had identical banding patterns). *Staph. epidermidis* (with a different DNA fingerprint) was subsequently cultured from swabs of the donor's arms. *Staph. epidermidis* was not grown from swabs taken after standard skin preparation. No failure in the donor arm cleansing procedure at the time of donating the implicated donation had been noted. The probable source of the recipient's bacteraemia was

concluded to be transfusion with platelets contaminated with skin flora from the donor's arm.

BAC8. One recipient (52 year old male) suffered a severe febrile reaction during transfusion of a leucodepleted, 3 day old apheresis platelet unit, and died later the same afternoon. On inspection the next day the remainder of the platelet pack had some signs of bacterial contamination (unusual orange colouration and small specks visible when held up to the light). *Escherichia coli* was cultured from the recipient's blood and from the platelet pack (and these two isolates had identical biochemical profiles). No leaks or defects were identified in the platelet pack. An interview with the donor confirmed absence of symptoms of infection at and around the time of donation and swabs of the donor's arm skin were negative on culture. The probable source of the recipient's reaction, and cause of death, was concluded to be transfusion with platelets contaminated with *E.coli*. No source of the contamination was identified.

BAC9. One recipient (78 year old female) suffered symptoms including feeling hot, sweaty and dyspnoeic during transfusion of a pooled, leucodepleted, 4-day-old platelet unit. The recipient subsequently recovered and was completely asymptomatic two weeks after the transfusion. Blood cultures were not taken from the recipient. *Staphylococcus epidermidis* was cultured from the platelet pack and from the red cell unit made from the same donation. An interview with the donor confirmed absence of symptoms of infection at and around the time of donation and swabs from the skin of the donor's arm were negative on culture. The probable source of the recipient's transient reaction was concluded to be transfusion with platelets contaminated with *Staph. epidermidis*. No source of the contamination was identified.

BAC10. One recipient (63 year old female) developed urticaria, rigors and pyrexia during transfusion of a pooled, leucodepleted, 4-day-old platelet unit. The recipient was pyrexial for three days after transfusion and was treated with broad-spectrum antibiotics. *Bacillus cereus* was cultured from the recipient's blood and from the platelet pack (and these two isolates were both of type 29). *B cereus* (type 29) was also cultured from swabs from the skin of the donor's arm (both pre- and post- arm cleansing). The probable source of the recipient's reaction was concluded to be transfusion with platelets contaminated with *B. cereus* from the donor's arm.

BAC11. One recipient (58 year old female) suffered a respiratory and cardiac arrest during transfusion of a second unit of red cells (33 day old, not leucodepleted) and died the same day. *Yersinia entercolitica* (serotype 09, biotype 3) was isolated from the patient's blood, the implicated red cell pack, and the archive of the implicated donation and a fresh sample of blood taken from the donor 5 months after the donation. On follow-up the donor reported a history of diarrhoea a few weeks prior to the donation. The probable source of the recipient's reaction, and cause of death, was concluded to be transfusion with red cells contaminated with *Yersinia entercolitica* from the donor's blood.

The four cases BAC7-10 were associated with leucocyte-depleted platelets since all platelets issued in the UK were leucocyte depleted. The numbers of cases before and after universal leucodepletion were too small to detect any effect of leucodepletion on bacterial contamination of components.

Other

HAV1. One transfusion transmitted HAV infection was reported. The recipient was traced and tested for HAV infection, one month after transfusion with three red cell units, after a donor reported HAV infection that developed ten days after donation. An HAV infectious donation collected from a donor during acute (asymptomatic) infection was concluded to be the probable source of HAV infection for one recipient[2]. The recipient of the platelets from the implicated donation was found to be non-immune and not infected.

MALARIA1. One transfusion transmitted malaria (*Plasmodium falciparum*) infection was reported. The recipient developed cerebral malaria two weeks after transfusion with two red cell units and died within two weeks of diagnosis. One new donor was found to have malarial antibodies when a subsequent sample was tested.

Morbidity and mortality of recipients with transfusion transmitted infections

The majority of recipients with transfusion transmitted infections suffered serious morbidity as a result of their infection. Table PTI 5 shows the breakdown of cases by morbidity and by infection. Major morbidity was defined as acute symptomatic confirmed infection or persistent viral infection. Minor

morbidity was defined as asymptomatic resolving viral infection. As such "minor" infections would only be diagnosed incidentally, it is not that surprising no reports - predominately originating because of clinical disease - fall into this category.

Table PTI 5 Morbidity by infection for transfusion-transmitted infections, 1995-1999.

	TTIs								All PTIs	
	HAV	HBV	HCV	HIV	Bacteria	Malaria	Total	Mean age(SD) [range]	N	Mean age(SD) [range]
Death attributed to infection	0	0	0	0	3	1	4	55(19) [32-78]	10	57(27) [0-85]
Death due to underlying condition	0	1	0	0	1	0	2	[20, 72]	4	51(25) [20-72]
Major morbidity due to infection	1	4	2	1	7	0	15	50(24) [4-80]	81	47(22) [0-84]
Minor morbidity due to infection	0	0	0	0	0	0	0	-	0	-
Patient outcome not known	0	0	0	0	0	0	0	-	12	53(19) [4-75]
Total	1	5	2	1	11	1	21	51(23) [4-80]	107	49(22) [0-85]
Mean age(SD) [range]	80	51(22) [26-72]	[61, 79]	46	42(24) [4-77]	78				

The average age of these recipients was 51 years (St dev of mean: 23, 95% confidence interval: 41-61, median: 58, range 4-80 years) and was similar to the age of all recipients reported with post-transfusion infections (mean: 49, St dev of mean: 22, 95% confidence interval: 45-53, median: 50, range 0 to 85 years).

Details of post-transfusion infections not found to be transfusion transmitted infections

Sixteen (15%) post-transfusion infections (5 Bacteraemia, 3 HBV infection, 7 HCV infections and 1 HIV infection) were classified as post-transfusion infections of undetermined source due to incomplete investigation of the transfusion(s) implicated as the source of infection. For 58 (54%) post-

transfusion infection reports (26 HBV infections, 25 HCV infections, 3 bacterias, 3 HIV infections and 1 HAV infection), investigation was completed and no evidence was found to implicate transfusion as the source of infection. A probable source of infection other than transfusion was identified for 31 of these infections.

Reporting delay

For the 11 transfusion-transmitted bacterial infections, symptoms occurred on the same day as the transfusion. Blood centres were informed of the bacteraemias suspected to be associated with transfusion on the same day (n = 7), the next day (n = 2), 2 days (n = 1) and 7 days (n = 1) after transfusion. The median interval between the initial information being reported to the blood centre and the completion of the initial surveillance report form by the blood centre was 32 days (mean 57, St dev 65, range 3-228).

Four of the transfusion-transmitted viral infections (1 HAV, 1 HBV and 2 HCV) were diagnosed with sub-clinical infections (45 days, 130 days, 224 and 440 days after transfusion respectively) during the follow up of suspected infectious donations. The other five transfusion-transmitted HBV infections and the malaria transmission were diagnosed with infection 86, 98, 141, 455, 2303 (HBV) and 42 (malaria) days after transfusion. The median interval between the initial information being reported to the blood centre and the completion of the initial surveillance report by the blood centre form was 64 days (mean 73, St dev 45, range 16-127). Some of this period of time – at least in some cases – was whilst confirmation of the recipient's infection details was awaited.

Underreporting

The cases ascertained by this surveillance system were diagnosed, suspected to be attributable to transfusion, communicated to the blood service, and reported by a blood centre to the surveillance centre. At any one of these steps, other post-transfusion infections may have been missed and the extent of underreporting of post-transfusion infections is therefore unknown. The proportion of post-transfusion infections that are reported each year may vary as other factors such as testing performed on transfusion recipients, awareness

of transfusion as a possible source of infection, reporting of information to blood centres and reporting of information from blood centres to the surveillance centre vary.

3.3 Discussion

Donation testing

A system for collecting standardised data about routine donation testing for four serological markers of infection has been established. Data about reactivity rates and infection rates are available. The identity of every positive donation is collected to enable matching with infected donor reports and monitoring of infected donor reporting rates.

Testing specificity

The specificity of donation testing was high - less than 0.3% (1 in 333) of donations were referred for confirmatory testing due to false reactivity to the full suite of screening tests. There was an increase in repeat reactivity to HBsAg tests amongst repeat donors that was associated with a poorly performing batch of test kits from a single manufacturer.

Removing tests performed on donors who were being monitored because of past reactivity to tests from the data removed the dependence of repeat reactivity rates in repeat donor donations on variations in the policy on bleeding these donors.

Some misclassification of donor type is expected to occur in the donation testing data. Some misclassifications are identified when infected donor reports are matched to donation testing data and contain information that allows re-classification of donor type. However, as the small changes in the numbers of donations tested in each donor category have little effect on rates, this misclassification is not expected to cause any important errors in the data.

Infection rates in blood donations

The overall rates of infected donations in England and Wales were low and rates were much lower in donations from repeat donors than in new donors.

Most donations of blood (89%) came from repeat donors. HIV antibodies were detected in 0.86 per 100,000 donations tested in England and Wales. Comparative data from other European countries shows rates per 100,000 donations of 2.41 in France (1995), 1.49 in Germany (1993), and 0.28 in Finland (1995) (WHO, 1996). HCV antibodies were detected in 0.05% of donations from new donors in England and Wales, compared with 0.28% in France (1994), 0.16% in Germany (1995), 0.05% in Finland (1995) and 0.04% in Denmark (1995) (Naplas, 1996). Difference in the recruitment and selection of donors, as well as differences in the prevalence and incidence of infections in the general population, affect the rates of infection in donations of blood. The tests that are used also affect these rates: for example, in the UK, blood donations are tested for HBsAg whereas in Denmark and France, blood donations are tested for HBsAg and antibody to hepatitis B core antigen.

There was a significant trend (at 5% significance level) to increasing anti-HCV prevalence in donations from new donors at the very end of the study period, and a significant decrease in anti-HIV prevalence in donations from new donors (Figure 3.4). However, although a trend was identifiable (at the 95% confidence level) neither of these trends were strong. Annual data for HCV prevalence in new donors from 1995 to 2000 show a significant ($p<0.01$) downward trend.

Monthly analysis of donation testing data

Monitoring of donation testing data and of all observed centre and donor type specific infection rates identified by analyses as outside the probable range (at the 5% significance level) based on the previous 3 years' data allows deviations in the data to be noticed. Many of the unusual results identified by the monthly analyses were relatively minor fluctuations that required no follow-up. Deviations that meet certain criteria can be highlighted for further attention. The first year of analyses has allowed criteria for further attention to be set at a workable level.

None of the unusual results identified during this first year of running these analyses, have identified a problem with donation testing or been connected with an outbreak in the general population. Two documented outbreaks of syphilis infection occurred in England during this time period (CDR,1998; CDR,

1999). Both these outbreaks predominately affected individuals in high-risk groups: none of the individuals linked to these outbreaks were identified though blood donation testing. The performance of the analyses in the event of an outbreak that does involve blood donors was not observed (upto August 2000).

The analyses supplement the usual vigilance of unusual infections. The analyses would not identify outbreaks that do not result in significant changes in rates of infection. The occurrence of a single acute HBV infection in a blood donor would be unlikely to significantly change the rate of HBsAg positivity in blood donations but can warrant an outbreak investigation - for example if the individual who is infected has an identified risk that may have also affected other individuals (e.g. a recent invasive medical procedure), or if others are likely to have been exposed to the infected individual (e.g. a health care worker performing exposure prone procedures). These analyses would be unlikely to identify small but important changes in the number, or proportion, of infections that were acquired recently or between donations i.e. acute infections and seroconversions.

These routine analyses have the potential to identify changes in test performance and changes in the frequency of infected blood donors that may be important. Further investigation of changes in test performance may lead to identifying bad test batches or operational problems. Further investigation of changes in infection frequency may lead to identifying an outbreak of infection or a failure in donor selection at a local or national level.

Criteria for defining results that warrant further attention may be changed in the light of further experience.

These analyses continue to be run each month. Reporters and other relevant staff within the blood service and the Public Health Laboratory Service will be informed of any results that meet the criteria for further attention.

Infected donors

A system for collecting standardised data about blood donors found to have HBV, HCV, HIV or Treponemal infections on donations testing has been established. Data about demographic characteristics, previous donations, and risk factors for infection are available. Anonymous identifiers enable matching

with other sources of data about these infections, such as laboratory reports, and AIDS case reports to PHLS CDSC.

Anti-HCV was the most prevalent marker of infection in blood donors in England and Wales (1995-1999), followed by HBsAg, treponemal antibodies and, least frequently, anti-HIV (Table 3.6).

There was a decrease in the prevalence of anti-HCV in donations from new donors, and in donations from repeat donors during the years 1995-1999. Almost two-thirds of anti-HCV positive donations from repeat donors during this period of time (starting four years after the introduction of anti-HCV testing) were from donors who were being tested for anti-HCV by the blood service for the first time (compare numbers of "new" and "repeat" positives in Tables 3.6 with "newly tested" and "previously tested" respectively in Table 3.12). The decline in the prevalence amongst donations from repeat donors is largely due to the removal of these positive individuals from the donor panel. The decrease in prevalence amongst donations from new donors may be due to a decreasing prevalence in the population or due to improved donor selection. The process of donor selection has been changed and expanded during this period (see Chapter 2) – and this was in fact partly motivated by the finding at the start of anti-HCV testing of a large number of anti-HCV positive donors reporting a history of injecting drug use. It is therefore likely that improvements in donor selection are responsible for a decrease in anti-HCV prevalence in new donors. As documented in Chapter 4, the recent incidence of anti-HCV in repeat blood donors is extremely low. If incidence was greater in the past, there may also be a truly decreasing prevalence in the population of new donors – typically younger individuals than repeat donors – who present to give blood each year.

The biggest difference in the epidemiology of infection in blood donors and in the general population is the frequency of infection – shown by both the relatively low prevalence and relatively low incidence. For example the prevalence of anti-HIV infection in antenatal women outside London during 1999 was 0.02%, (UASSG, 2000), 4.7-fold that observed in new donors in England and Wales (i.e. including London). The prevalence of HBsAg in samples from hospital patients (15-44 years old, excluding those requesting HBV testing) collected in 1996 from 16 microbiology laboratories in England and Wales was 0.37% (Gay NJ, 1999), over 11-fold that observed in new donors.

Also, the characteristics of infected blood donors differ from the characteristics of many other groups of diagnosed individuals due to the pre-selection of individuals to give blood – particularly the selection of healthy individuals and the selection of individuals who are not at known high risk of infection. For example, the relatively low proportion of HIV infections acquired by injecting drug use (1% (n=1) compared to 9% (n=3,608) amongst all reported anti-HIV positive diagnoses reported to PHLS CDSC (up to June 2000) (CDR,2000). The distribution of probable routes of infection reported for infected donors differed quite markedly from that observed amongst all reports of newly diagnosed infections. The most common risk factors for HIV, HBV and HCV were present amongst infected donors, however they accounted for a much smaller proportions of infections than in other tested groups. For many of these risk factors (e.g. sex between men, injection drug use) donor selection aims to specifically exclude donors with these risk factors. The relative infrequency of these risk factors in infected donors suggests that this is successful, however, there may also be an information bias in the reported risk factors – with donors more likely to withhold information about exposure histories that should have excluded them from donating blood. Follow-up by the PHLS CDSC HIV/AIDS Centre did identify a probably route of infection that should have led to permanent exclusion from donating blood for 7.5% (N=7) of anti-HIV positive donors who did not report this route to the blood service.

The selection of low risk individuals to be blood donors, and the resulting distribution of probable routes of infection acquisition in blood donors biased towards low risk exposures and no known route of infection, can be useful for pubic health work. Low risks for infection, and unusual routes of infection, are relatively more likely to be observed amongst donors, who therefore can act as a sentinel group for infections in groups with exposures believed to be of low risk, for example sex between men and women in the UK with partners with no identified increased risk for HIV infection. Donors with no identified risk of infection, or with reported exposure histories that are of uncertain risk, for example sexual exposure as a reported source of HCV infection, may also be good subjects for studies to identify unrecognised risk factors and evaluate exposure histories of uncertain risk. For 46% of HBsAg positive donors (detected between 1/10/95 and 30/6/96) no exposure associated with an increased risk of HBV infection was identified. During the same time period,

there was no exposure associated with an increased risk of HCV infection identified for 14% of anti-HCV positive donors, and, for a further 28% of anti-HCV positive donors, a *possible* exposure, of unknown risk, was identified. These possible risk factors included sexual contact with a partner with no known HCV infection or known increased risk of HCV infection, possible contact with blood during acupuncture, body piercing, invasive medical/dental procedures, and possible occupational contact with blood: these are common exposures that may be coincidental with, rather than associated with, infection. Whether these possible exposures represent true risks for infection could be determined by analytical epidemiological studies, for example case-control studies, providing enough such cases (and suitable controls) are available for study.

Some strong features of the epidemiology of these blood-borne infections show clearly amongst blood donors despite the selection biases in this population. The predominance of individuals with non-white ethnicity amongst HBsAg positive individuals (Table 3.10) and the high proportion of HCV infections acquired by injecting drug use (Table 3.12) have been frequently observed in other groups and are well known features of the epidemiology of these viruses. The excess of males amongst all infections has also been observed in other surveys, for example amongst hospital patients the prevalence of HBsAg carriage was 0.63% in males, 0.15% in females (Gay NJ, 1999). Available denominator data show that approximately half of all donations (45% of donations from new donors and 52% of donations from repeat donors) are collected from male donors. Should this change, to collect a larger (or smaller) proportion of donations from male donors, we would expect to see an increase (or decrease) in the prevalence of infection in donations. The sex ratio amongst donors is clearly important when comparing the prevalence of infection found in different surveys. The higher prevalence of blood-borne infections observed in some other European blood services might be at least partially accounted for by a higher proportion of donations from male donors.

The age and sex distribution of HBsAg, anti-HCV, anti-HIV and Treponemal antibodies differ (Table 3.7 and Figure 3.6). HBsAg positives include donors with acute HBV infection and donors with chronic HBV (carriage), however as acute infection is relatively uncommon the pattern of this

age-distribution is predominantly that of HBV carriage. A study of the prevalence of anti-HBc (i.e. a marker of having been infected with HBV) amongst a large sample of donations collected at two blood centres in 1995 found anti-HBc prevalence increased steadily with increasing age, and again was significantly higher in males (Soldan K, 2000). If this peak is due to a cohort of donors infected with HCV in the past that are now passing through the donor population, and incidence of infection is now much lower, we would expect to see (all other things being constant) a continuing decrease in the prevalence of anti-HCV in donations from new donors.

HIV infected donors had both a lower peak age group, and a significantly lower average age (Table 3.9) than the donors with other infections. Donors found positive for treponemal antibodies were the oldest group of infected donors, and the only group to show a steady increase with increasing age across the whole age span. As the majority of these donors have persistent markers of past infection this pattern is to be expected as both the time at risk of exposure increases with age, and syphilis infection was more common in the past. As for HBV, there are some cases of acute syphilis amongst these data. Cases of recent infection are the most important for both the blood service and for providing public health information, but are relatively few in number compared to past infections and so not well described by the data presented here. Further work is needed to ensure that infected donor reports specify when the donor has acute syphilis, and to monitor this sub-group of donors separately so that any small but important changes in their frequency, or characteristics, are not overlooked.

Interpretation of the ethnic groups of infected donors is very limited by the lack of data about the denominators of donations tested from donors in each ethnic group. The proportion of donations collected from ethnic minorities is known to be relatively small compared to the proportion of the total population in these groups, but exact data were not available. In an attempt to obtain some information about the proportion of donors who are of Asian ethnicity, a computer programme (NAMPECHAN) that was developed by Bradford County Council to identify names of Indian sub-continent origin (and their religion and language) has been applied to a cohort of 40,000 new donors (work not included in this thesis). This was also applied to HBsAg positive donors and the results indicated the prevalence of HBsAg in donors with a South Asian name

was 7.5 times higher than in the rest of the donor population. This supports the picture of HBsAg association with non-white ethnicity seen in Figure 3.9 a) when compared to the other infections (i.e. in Figure 3.9 b), c) and d)). HIV infection and treponemal antibodies appear (in the absence of denominator information to confirm this) to have an association with black ethnic groups. The association of HIV infection in England and Wales with having lived in sub-Saharan Africa is well documented. Between 5 and 10% of donors with positivity for treponemal antibodies report a past history of Yaws, a tropical ulcerative disease caused by a treponemal infection, and probably responsible for at least some of the association of this test result with African ethnicity.

The data in Tables 3.14 and 3.15 show that most infectious donations are from individuals who do not report exposure histories that should have led to their exclusion from donating blood. The collection of infectious donations from donors with a risk factor that occurred over twelve months ago could be avoided by lifetime deferral of these donors from blood donation. However, as the risk factors in the "12-month exclusion" category tend to be relatively common in the potential donor population life-long deferral may mean the loss of an unacceptable number of donations – the vast majority of which are expected to be from un-infected donors. The collection of infectious donations from donors with risk factors that should have excluded them from donating blood indicates failures either in the communication, understanding, or compliance with, donor selection criteria. In some cases, the donor may be unaware of their risk at the time, for example if the donor was unaware of a sexual partner's infection or risk of infection. These donations are extremely difficult to prevent. In other cases, donors are both aware of their risk and of the selection criteria but do not comply with the blood service's request to not give blood. A small sample of reasons for this is given in Table 3.15 and collection of these data continues. As the blood service has to rely on donors to comply with selection criteria, this is a vulnerable point in the process of providing a safe blood supply and deserves ongoing monitoring. Donors' perception of the blood service, and their trust in its staff and systems may affect their compliance with donor selection as well as their response to donor recruitment. These data may be used to monitor the compliance of various risk groups with donor selection, and to identify risk groups who are not aware of, or not minded to comply with,

donor selection criteria so that communication can be targeted at the groups in which donor selection is most often failing.

Transfusion-transmitted infections

A system for collecting standardised data about all post-transfusion infections that blood centres are informed about has been established. Data about demographic characteristics, the transfusion episode, clinical consequences of infection and other risk factors for infection are available. Anonymous identifiers enable matching with other sources of data, (e.g. laboratory reports) about these infections.

Reports have been received from most centres. Many hospitals have not reported any cases, however reports have originated in hospitals all over the country and most reporting hospitals (and reporting hospital clinicians) have reported just one case. There were no large clusters of cases associated with any one reporting individual or hospital. This distribution of reports suggests that the mechanisms for hospitals to notify blood centres are in place all over the country, and that there are no serious biases in reporting.

Reported transfusion-transmitted infections are rare: only 21 confirmed cases were recognised during this 4-year period of reporting. Investigations of a further 87 cases of post-transfusion infection were reported. Half (54%) of the PTI reports have been shown not to be caused by transfusion. For 15% of the reports the investigation was inconclusive and for the remainder investigation continues. Exclusion of transfusion as the source of infection and dissemination of this information can have useful infection control implications as other sources of infection – perhaps assumed to be unlikely at first - may then be further investigated and, if identified, become the subject for infection prevention. This has been the case in some hospital-acquired hepatitis infections eventually associated with infected health care staff.

Twenty-three cases of post-transfusion reactions suspected (but not confirmed) to be due to bacteria were also reported. Conclusive investigation of a suspected bacteraemia in a transfusion recipient relies heavily on the collection and handling of relevant samples at the hospital where the transfusion was performed. This means that absence of evidence of an

infection (or toxin), in donations given to recipients who had post-transfusion reactions that were suspected (on clinical presentation) to be due to bacteria does not equate with evidence of absence of a transfusion-transmitted infection (or toxin).

The intervals between transfusion and diagnosis of transfusion-transmitted infections were long - many weeks, months or years. Infections transmitted by transfusion between 1/10/95 and 30/9/99 will continue to be ascertained by the surveillance system as diagnoses are made in the future.

The delay in reporting (1 to 2 months) suggests that the data are not timely enough to act as early warning of outbreaks of transfusion-transmitted infections e.g. as a result of a batch of contaminated blood packs. (Parallel reporting of incidents that indicate a break down in quality assurance acts as a mechanism to quickly detect such problems.)

Four transfusion-transmitted viral infections (1 HAV, 1 HBV and 2 HCV infections) were detected by follow-up of recipients after the detection of infections in blood donors. In one case of HAV the donor reported an HAV diagnosis shortly after donating blood. In two cases of HCV infection the donor's infection was diagnosed by the blood service by the testing of a subsequent donation. In one case of HBV the donor's GP informed the blood service of the donor's infection. None of these transfusion-transmitted infections had caused symptomatic, diagnosed disease in the recipients. Two of these transfusion-transmitted infections (1 HBV and 1 HCV) were due to a donation collected from a donor during the marker negative "window period" early in a recent infection. One (HCV) was due to a laboratory error resulting in a false negative test result. One (HAV) was due to an infection for which no routine microbiology testing is performed.

Eleven transfusion-transmitted bacterial infections were due to collection of a donation from a donor with an infection for which no routine microbiology testing is performed.

Four transfusion-transmitted infections reported during this period resulted in the death of the recipient (3 bacteria, 1 malaria).

Several reports have been received of components that were observed to have visual signs of bacterial contamination before use, were not transfused, were sent for bacteriological investigation and were found to contain bacteria expected to cause disease in a recipient if transfused. Inspection of

components (especially platelets) detected contamination and prevented morbidity in these incidents. Such inspection is encouraged. These reports indicate "near-miss" bacterial transmissions. The investigation of the source of the contamination in these cases can be as informative as the investigation of transmissions, and the possibility of requesting and collating some information about these cases in the future is being considered.

An unknown, but probably relatively large, proportion of transfusion transmitted infections are expected to be clinically unimportant, and undiagnosed - at least for many years and the extent of under-diagnoses of clinically important transfusion transmitted infection, and of underreporting of diagnosed infections to blood centres and to CDSC is not known.

Based on the cases reported the following recommendations have been made:-

- National collation of data arising from these cases needs to continue over several years before a picture of the extent and nature of the infectious complications of transfusion can emerge.

- Clinicians should report all post-transfusion infections diagnosed in their patients to the blood service (via their regional blood centre) for appropriate investigation. Blood centres should, in turn, complete an initial report form as soon as possible.

- The quality of investigation of transfusion reactions suspected to be due to bacteria is variable. Hospitals should consult guidelines and the blood service about the investigation of such cases, including the sampling and storage of implicated units. National guidelines (from the NBS) on the investigation of these cases are currently being revised following comments from users.

- Donors' clinicians (and donors themselves) can aid the detection of transfusion-transmitted infections, and hence their appropriate care, by communicating with the blood service about any relevant history of blood donation on diagnoses with blood borne infections.

3.4 Summary and Conclusions

Surveillance of infections in blood donors and in blood recipients has benefits for transfusion medicine and for general infectious disease control and epidemiology. The surveillance system established in England and Wales built on the existing systems in the National Blood Service for monitoring donation testing and on the existing systems in the PHLS for disease specific infection surveillance, to enhance the surveillance of transfusion transmissible infections. Data about donation testing, frequency of infections, characteristics of infected donors, frequency of recognised transfusion-transmitted infections and characteristics of transfusion-transmitted infections are collated, analysed and disseminated regularly.

These data have demonstrated that the prevalence and incidence of HBV, HCV and HIV in blood donors in England and Wales during 1996-1999 were low and fairly stable. Over the total time period (1995-1999) there were significant trends towards decreasing anti-HCV prevalence in donations from new donors, and decreasing anti-HIV prevalence in donations from new donors, however the strength of these trends was no greater than have been observed for other similar length periods that are not significant when longer time periods are analysed.

No outbreaks of infection or crises in test performance were detected by the surveillance over the period of time described here, but analyses were designed and implemented that have the potential to identify these through irregularities in donation testing results.

Detailed reports were received for 98% of infected donations detected in England and Wales. Risk factor information was available from the NBS for 76% of all infections, and was obtained via the PHLS CDSC for 65% (20/31) of the anti-HIV positive donors who did not provide information to the NBS. Collection of data about each infected donor allowed identification of donors who had seroconverted for HBsAg, anti-HCV or anti-HIV between donations and therefore enabled estimates of incidence to be made. Further work will investigate factors associated with seroconversion.

Information about the probable route of infection has been collected in a standard format for every reported infected donor and enabled comparison of the risk factors for the different infections.

Only 20% of post-transfusion infections were concluded after full appropriate investigations to be transfusion-transmitted infections. Just over half of the cases concluded to be caused by transfusion (11/21) were due to bacterial contamination of transfusions. HBV was the most common transfusion-transmitted viral infection reported. Transfusion-transmitted HBV, HCV and HIV infections occurred due to the following occurrences: donation in the early stages of infection (without the marker of infection used in testing), donation in the tail-end stage of carriage of HBV infection, false negative test results due to error in the laboratory. Two non-bacterial infections for which blood is not tested also occurred (HAV, malaria). The frequency of recognised, reported transfusion-transmitted infections was shown to be very low, and to be low relative to the number of reports of non-infectious complications of transfusion. However, the extent of underreporting of transfusion-transmitted infections is not known and may be greater for many infections than it is for non-infectious complications that are fast and acute in onset after transfusion.

The surveillance system for transfusion-transmissible infections in England and Wales is an ongoing, systematic, collation of data that are analysed and disseminated to those in charge of control and prevention of transfusion-transmitted infection, and infections in the general population. The data held in the surveillance databases provides a baseline for future monitoring of the epidemiology of transfusion-transmissible infections and holds potential for both descriptive and analytical epidemiological studies.

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4.1 Introduction

Studies that provide specific analyses and estimates have been conducted using data from the surveillance system, and additional information specially collected for the purpose of the further study. Two of these studies are described below. The first collected further information about donors who appeared – from the surveillance reports – to have seroconverted for anti-HCV and determined the incidence of HCV infection amongst repeat donors in England during 1993 to 1995. The second collected further information from blood centres about all acute HBV infection reported to PHLS between 1991 and 1997 as associated with transfusion and described the frequency of confirmed transfusion-transmitted cases and the reasons for HBV infectious blood entering the blood supply.

4.2 Survey of HCV seroconversions in blood donors: England, 1993-95.

Introduction

In September 1991, UK Blood Transfusion Services began routinely testing all blood donations for antibody to hepatitis C virus (anti-HCV). Since

then, approximately 2 million healthy adults have been tested for anti-HCV annually by the English National Blood Service (NBS). National collation of test results, and of characteristics of anti-HCV positive donors, provides valuable information about the donor panel, and about a selected sample of the adult population of England.

The majority of acute HCV infections are asymptomatic, and most probably pass undetected. An anti-HCV positive donation, preceded by an anti-HCV negative donation, suggests recent infection. The testing of donations from repeat donors therefore provides a rare opportunity to identify incident HCV infections. Information about incident HCV infections is of interest to blood transfusion services and to public health workers as it relates to current, rather than past, HCV transmission. Pre-donation selection of blood donors aims to exclude donors who have recognised risks for contracting blood borne infections. Incident infections in blood donors usually indicate one of three scenarios: a failure in the definition or application of pre-donation selection criteria; an unrecognised exposure to blood borne infection, or infection through an exposure that is not included in pre-donation selection criteria because it is a frequent exposure of blood donors and thought to be associated with a relatively small risk of infection. There remains a small risk of transmission of HCV by transfusion due to anti-HCV negative, infectious donations and due to failures in the testing and exclusion of seropositive donations. The number of donors who seroconvert for anti-HCV between donations is one piece of information needed to estimate the risk of collecting a donation from a recently infected donor who has not yet developed detectable anti-HCV, and hence the risk of transmitting HCV infection by transfusion.

A survey of seroconversions for anti-HCV detected by English blood centres from September 1991 to December 1995 was conducted during 1994/95 and the results of this survey have been used, along with data from the infection surveillance system of the National Blood Authority and Public Health Laboratory Service Communicable Disease Surveillance Centre (NBA/PHLS CDSC), to estimate the rate of seroconversion for anti-HCV in repeat donors in England during 1993-1995.

Subjects and methods

Sample

Blood donations in England are obtained from voluntary unpaid donors. Pre-donation selection excludes individuals who are outside the age-range 18-65 years, have had known high risk exposures for contracting blood borne infections, or have any medical condition which contraindicates either the loss of 450ml of blood, or the giving of their blood to patients. The number of repeat donors in 1994 constituted approximately 4% of the 18-65 year old population of England in the middle of 1994.

During the study period all donations were tested for anti-HCV using enzyme-linked immunosorbant assays (ELISAs). Initially-reactive donations were re-tested by ELISA. Donations that were reactive on repeat testing were not issued and supplementary tests (additional ELISAs and recombinant immunoblot assays (RIBAs), and, in some cases, polymerase chain reaction (PCR) for HCV DNA)) were performed to clarify the infection status of donors.

Donors with evidence of HCV infection were contacted by the blood centres and were offered additional testing and counselling by the blood centre followed by referral to a relevant medical specialist, or were referred to their general practitioner for further management (Ryan KE, 1994). Risk factors for HCV infection were discussed with donors during their follow up and any acknowledged by the donor were recorded.

Case definition

A standardised algorithm for confirmatory testing of blood donations was not used during the study period and variation in the tests used had to be accommodated. In order to include all true biological seroconversions but exclude any spurious "seroconversion" caused by changes in test format and performance over time, or due to false reactivity in the tests, a comprehensive case definition was developed and agreed. (Box 3)

Box. 3 Criteria for determining seroconversion for anti-HCV.

Pre-seroconversion donation		Post-seroconversion donation		
RIBA 3.0 non-reactive	and	RIBA 3.0 positive	}	
			}	
	or		}	not PCR negative
ELISA non-reactive & RIBA 2.0 non-reactive	and	ELISA (of same manufacturer and generation as pre-seroconversion test) positive & RIBA 2.0 positive	} and	**if** < 12 months after pre-seroconversion donation
	or		}	
ELISA 3.0 non-reactive	and	ELISA 3.0 positive & RIBA positive	}	

Methods

In July 1994 all English blood centres were asked to return information about the tests performed and results obtained on the first anti-HCV positive donation (i.e. post-seroconversion donation) and the last anti-HCV negative donation (i.e. pre-seroconversion donation) for each donor considered to have seroconverted for HCV between donations since anti-HCV testing began in 1991. Seroconversions identified after July 1994 were also reported and included in the survey. Information was also requested about possible exposures to HCV infection. In October 1995 the national system for the surveillance of donation testing was revised and seroconversions were then identified from routine surveillance reports.

Test results were examined to see if they met the case definition. If they did not, the reporting blood centre was contacted and asked for any additional test results or to perform additional tests on archived samples - most commonly they were asked to perform parallel RIBA tests on samples from pre- and post-seroconversion donations. Follow-up of missing returns, and requests for additional information continued during 1995.

During 1991 (September-December) and 1992 the majority of repeat donors tested for anti-HCV were being tested by the NBS for the first time. As a previous negative anti-HCV test is a pre-requisite for HCV seroconversion, rates for 1991 and 1992 were not calculated.

The rate of post-seroconversion donations in all donations from repeat donors was calculated by dividing the number of seroconversions by the

number of donations from repeat donors. The numbers of donations from repeat donors tested for anti-HCV during 1993, 1994 and 1995 was obtained from the national system for the surveillance of donation testing. The incidence of HCV seroconversion was calculated by dividing the number of seroconversions by the number of person years (PYs) at risk. The number of PYs was estimated by dividing the number of donations from repeat donors by the average annual number of donations per repeat donor. The average number of donations per repeat donor at one blood centre (that tests 5% of the repeat donor donations in England) was 1.71 over a one-year period, and 3.49 over a three-year period (1993-95). The average annual number of donations during the three-year period 1993-95 was therefore taken as 3.49/3 = 1.16: this is equivalent to an average interval between donations of 0.86 years.

Table 4.1 Seroconversions for anti-HCV amongst repeat donors in England 1993-1995.

	1993	1994	1995	1993-1995
Number of donations from donors who have seroconverted for HCV since a previous donation	5	3	6	14
Number of donations from repeat donors tested for HCV antibody	2,140,712	2,116,178	2,105,038	6,361,928
Frequency of donations from donors who have seroconverted for HCV since a previous donation	1 in 428,142	1 in 705,393	1 in 350,840	1 in 454,423
Rate of seroconversion per 100,000 PYs (95% confidence interval)	0.40 (0.17-0.96)	0.24 (0.08-0.75)	0.49 (0.22-1.08)	0.26 (0.15-0.43)

Results

Twenty-three reports of putative HCV seroconversion in repeat donors tested between September 1991 and the end of 1995 were received. The test results available for 7 of these did not satisfy the case definition. As centres were asked to report only those donors for whom full testing information was available, these 7 reports do not represent all the possible additional cases of

recent HCV infection in repeat donors where the data is insufficient to satisfy our case definition. Two of the donors that fulfilled the study case definition for anti-HCV seroconversion were diagnosed during 1991 or 1992 and 14 of the cases were diagnosed during the study years, 1993-1995 (Table 4.1). The difference in the rates for 1993, 1994 and 1995 was not significant (p=0.59). PCR tests results were available for 10 of these 14: 9 were PCR positive, and one donor, whose first seropositive donation was taken two years after the last seronegative donation, was PCR negative. Five blood centres reported no HCV seroconversions. Three centres reported more than one HCV seroconversion: one centre in the Thames regions' reported 4 cases and had the highest rate of seroconversion; two centres, outside the Thames regions, reported 2 cases each. There was no significant heterogeneity between the rates by centre (deviance = 15.9, 13 degrees of freedom, p=0.25).

The average interval between donation of the pre-seroconversion and post-seroconversion donation for the fourteen cases was 1.29 years (median 1.38 months, range 0.42-2.33 years). This interval was 1.5 times the average inter-donation interval (1993-95) for all repeat donors.

The reported probable exposures to infection of the seroconverters are shown in Table 4.2, along with their sex and average age (information about ethnic group was not gathered). The approximate average age of all repeat donors was 40 years.

Table 4.2 Acknowledged probable exposures in donors who had seroconverted for anti-HCV.

Probable exposures to HCV infection	Donor selection criteria (1995) instruct exclusion	Number (%)of seroconverting donors		
		Total	Males	Females
Injecting drug use	Yes	2 (14%)	2	
Sex between men and women		5 (36%)	1	4
- known HCV infected partner	Yes[1]	1	1	0
- IDU partner[2]	Yes	2	0	2
- partner with tattoos	No	1	0	1
- partner from high HCV prevalence country	No	1	0	1
Blood contact with person with risk factors	No	1 (7%)	1	0
None identified	No	4 (29%)	2	2
No information	-	2 (14%)	2	0
Total	5 (36%) Yes 9 (64%) No	14 (100%)	8	6
Mean age (years) (95% confidence interval)		30.5 (26.6-34.4)	31.4 (26.1-36.7)	29.3 (21.1-37.5)

[1] At the time of donation this selection criterion was not in use (Kitchen AD, 1996).

[2] For 1 the partner was tested for anti-HCV, and found to be positive, after the donor's diagnosis, for the other the anti-HCV status of the partner is not known.

Discussion

English blood centres identified 412 anti-HCV positive repeat donors during 1993-1995. Very few (14) of these can be shown to represent incident HCV infections. This survey provides an estimate of the minimum rate of HCV seroconversion in repeat donors in England during 1993-95. The case definition for HCV seroconversion used in this study was chosen to exclude spurious seroconversion due to changes in test format and performance. The sensitivity and specificity of ELISAs and RIBAs used for anti-HCV testing changed between 1991 and 1995 with the introduction of third generation tests during 1993. By the time of this survey many of the archived samples from the pre-seroconversion donations under investigation had been used for repeat and supplementary tests, or discarded, according to each blood centre's protocols: repeat and supplementary testing of pre-seroconversion donations was therefore limited. By requiring evidence of comparably confirmed negativity for

the last seronegative donation, some cases of true seroconversion may have been excluded. Previous reports of HCV seroconversions with less strictly applied case definitions (Shopnick RI, 1995) have been quite justifiably challenged (Kessler C, 1995) and we chose to identify clear-cut, rather than probable, cases. Also, the survey was conducted retrospectively, and relied on retrieval of blood centres' records of tests performed on donations up to four years previously. For these reasons, this study may underestimate the number of seroconverting donors, and therefore the rate of seroconversion among repeat donors in England. Donations from repeat donors who were being tested for anti-HCV by the NBS for the first time during 1993-95 could not be excluded from the denominators that we used. A study conducted on donations during 1993 by one blood centre found 1.8% of donations from repeat donors to be from donors not previously tested for anti-HCV by the blood centre (Atrah, 1996). This inaccuracy in our denominator is likely to result in a further, although very slight, depression of the seroconversion rates as estimated from these data.

One blood centre has published reports about 3 donors diagnosed during 1993 (Atrah HI, 1995), and a further 4 donors diagnosed during 1994 and 1995 (Atrah HI, 1996) who were thought to have seroconverted for HCV. The blood centre obtained denominators of previously negative donors tested for anti-HCV during 1993 and estimated the seroconversion rate during 1993 to be 2.78 per 100,000 (1 in 35,937) previously negative, repeat donors (Atrah HI, 1996): more than ten-fold the estimate from our national study. However, the case definition used by this centre may have been flawed (Allain J-P, 1997 and Hewitt PE, 1997); only one of the cases described satisfied the case definition that we used. We consider the estimate of the HCV seroconversion rate in repeat blood donors derived by this single centre to be erroneously high.

Pre-donation selection criteria aim to select a sample of the population who do not report a recognised risk for blood borne infections prior to donation (Guidelines for the Blood Transfusion Services in the United Kingdom Section 1.1.5 Medical Assessment of Donors, 1997). Since the early 1980's potential donors have been given explanatory literature and since 1999, direct questioning about risk factors has been introduced for all new donors, and for donors who have not attended for two years or more. One centre has

additionally used a donor-completed questionnaire. The procedure for eliciting information about exposures to risks for HCV infection from infected donors has varied though out the UK. A standard questionnaire for interviewing donors is soon to be introduced. Information obtained post-donation from infected donors may be affected by both interviewer-related, and donor-related, biases. The majority of HCV infected blood donors have reported a history of injecting drug use (MacLennan S, 1994, Crawford RJ, 1994, Goodrick MJ, 1994, Neal KR, 1994, Gesinde MO, 1992 and Atrah HI, 1994), typically many years prior to donating blood. Almost one third of the HCV seroconverters in this study had no risk for HCV infection identified by the blood service. Testing the sexual partners of seroconverting donors may help to establish the true extent of heterosexual transmission in the donor population. Uncommon routes of transmission, and possible exposures that are not thought to be associated with risk of HCV infection, should also be investigated.

Seroconversion for HCV amongst repeat blood donors in England is very rare. This implies that the incidence of HCV in the population represented by repeat blood donors is now very low, and/or that pre-donation selection criteria effectively exclude most repeat donors with current exposure to HCV. During 1993-95, 14 donations (less than 1 in 450,000 donations), were obtained from donors who had seroconverted for HCV since a previous antibody negative donation. During the same period, 15 donations were obtained from donors who had developed detectable anti-HIV since their previous donation. The number of repeat donors who become infected with HCV, or other blood borne infections, but do not return to donate after their seroconversion cannot be ascertained by donation testing. In the future, tests for nucleic acids may enable detection of antibody negative, infectious donations.

The HCV status of the recipients of the seronegative, pre-seroconversion donations was not determined in this survey. Blood centres conduct tracing recipients of potentially infectious donations and one of the 14 pre-seroconversion donations has been shown to have transmitted HCV infection (Kitchen AD, 1996).

Donations from new donors contributed 12% of the total number of donations collected in England in 1993-1995. Seroconversion rates in new donors cannot be directly measured and there are reasons to expect that recent

infections in new donors may be more frequent than in repeat donors; repeat donors have been subjected to the post-donation selection criteria of negativity for tests for HCV, HBV, HIV and *T.pallidum* infection markers, and new donors may be more likely to donate blood in order to obtain testing following an exposure to infection.

Surveillance of donation testing and of donors who seroconvert for HCV between donations continues to be an important component of monitoring the safety of the blood supply. Study of possible exposures to infection that are associated with seroconversion for HCV, and of the course of HCV infection in seroconverting blood donors, who have a relatively precisely known date of HCV infection, should further contribute to our understanding of the epidemiology and natural history of HCV infection.

4.3 Review of acute HBV infection laboratory reports: Reports of acute HBV infection associated with blood transfusion in England and Wales, 1991-1997.

Introduction

Blood donations in England and Wales are collected from healthy donors who do not acknowledge factors associated with an increased risk of blood borne infections. All donations issued for transfusion (since early 1970's) have been found negative for hepatitis B surface antigen (HBsAg) as a marker of transmissible hepatitis B virus (HBV). These measures have resulted in low rates of HBV transmission by transfusion, but have not eliminated all infectious donations from the blood supply. HBV infections in recipients are investigated by National Blood Services (NBS) to identify if they were transmitted by transfusion, and prevent other transmissions, or to identify the need to explore sources other than transfusion. An implicated donation is concluded as having been probably infectious for HBV if it was:- i) collected from an HBsAg negative donor for whom there is evidence of acute infection at that time, or ii) collected from an HBsAg negative donor for whom there is evidence of infectious HBV carriage (i.e. antibody to hepatitis B core antigen (anti-HBc) present but antibody to HBsAg not, or weakly, present (Ilzuka H, 1992)), or iii) HBsAg positive (as shown by review of test results or re-testing of archived serum) and

erroneously released into the blood supply. Mutant HBV infections, not detected by routine HBsAg tests, also pose a risk of infectious donations being transfused (Jongerius JM, 1998).

Laboratories in England and Wales to PHLS CDSC report acute HBV infections, and the probable route of infection, voluntarily.

Methods and results

Acute HBV reports to CDSC were reviewed and information was sought from the NBS about reports associated with transfusion between 1991 and 1997 (Table 4.3). Between 1991 and 1997 24 of 4,185 (0.6%) acute HBV reports were associated with transfusion in England and Wales. For 10 reports, investigation by the NBS was either not feasible (e.g. donation identifiers not available) or inconclusive (e.g. one of more donor not traced for re-testing), or NBS information was not available retrospectively. Fourteen probably infectious donations identified by the NBS fell into two categories: 3 (21%) were collected from HBsAg negative donors during acute HBV infection and 11 (79%) were collected from HBsAg negative donors during late HBV carriage. No reports of erroneous release of HBsAg positive blood were identified.

Table 4.3 Acute HBV reports associated with transfusion, England and Wales, 1991-1997.

Year	Total reports[1]	Transfusion in UK as the most probable route of infection	NBS identified HBsAg negative probably infectious donor with		NBS investigation outcome not available, or inconclusive
			acute HBV	HBV carriage	
1991	572	5	0	2	3
1992	531	3	1	1	1
1993	629	5	1	4	0
1994	631	3	0	2	1
1995	613	5	0	1	4
1996	581	2	1	1	0
1997	628	1	0	0	1
1991-1997	4,185[2]	24 (0.57%)	3	11	10

[1.] Data at 31/3/98.

[2.] For 21 (0.50%) of these reports (1991-1997) the most probable route of infection was transfusion abroad (not known to have been confirmed by

investigation of the implicated donations), and for 3 reports no information about the place of transfusion was provided.

Discussion and conclusions

The NBS of England and Wales issue over 2.5 million donations annually. The cases presented here underestimate the number of transfusion-transmitted HBV infections: HBV is often asymptomatic and not all acute HBV infections are diagnosed and reported to CDSC.

Surveillance of acute HBV infections shows that transfusion transmission of HBV in England and Wales does occur, but is rare. The contribution of this route of transmission to the total burden of acute symptomatic HBV is small and acute infections in donors cause the minority of transfusion-associated cases. A similar breakdown of causes of transfusion-transmitted HBV was observed by North London blood centre during 1985-1993 (John Barbara - personal communication).

Donor selection criteria aim to exclude individuals with recent risk factors for the acquisition of blood-borne infection. Persistent HBV infections often follow perinatal or childhood infection and therefore are less likely to be excluded by donor selection.

Testing donations for anti-HBc, as is routine in some other countries, would have detected most of the HBsAg negative infectious donations identified. Since anti-HBc testing would also detect non-infectious donations from donors with naturally acquired immunity to HBV: further tests would be needed to avoid unnecessary loss of donations.

The post-transfusion infection surveillance that is described in Chapter 4, and that forms the infectious part of the Serious Hazards of Transfusion (SHOT) scheme (Williamson LM, 1996), will continue to monitor post-transfusion HBV infections. Policies to vaccinate multiply transfused individuals (Salisburg & Begg, 1996) remain justified. Testing of donations for anti-HBc has been considered but not adopted to date in the UK. The findings of this survey suggest that this now warrants further consideration of the costs and benefits, as anti-HBc testing could prevent the majority of transmissions from donors at the HBsAg negative tail end of HBV carriage. One caveat to this is that HBsAg tests have improved in sensitivity during the last 5 years, and the HBsAg

negative period at the tail end of carriage may now be much shorter than in the earlier years included in this survey. Of the five reports of transfusion-transmitted HBV infection to the PTI surveillance (1995-1999, see Chapter 3), only one was concluded to be due to a donor in the tail end of carriage.

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5.1 Introduction

Knowledge of the risks of transfusion transmitted viral infections is helpful in monitoring the safety of the blood supply and to evaluate the likely benefits of new strategies to improve transfusion safety. The current very low risk of transfusion-transmitted infections in the UK makes prospective study of transfusion recipients a prohibitively long and costly method to obtain accurate transmission rates (Table 1.2). Also, the results from direct observation are soon out of date as either the epidemiology of the infections considered, or transfusion service practices, change.

The advantages of estimating transmission risk using routinely available data and evidence-based assumptions include the speed and low cost, and the ease of revision in the light of new data or changing circumstances.

Generating estimates of the risk of transfusion-transmitted infections requires firstly identifying the circumstances that could allow an infectious donation to enter the blood supply, and secondly, assessing the likelihood of each, and then any, of the circumstances occurring.

In the UK, during the entire period of this study, all blood donations were tested for hepatitis B surface antigen (HBsAg), human immunodeficiency virus

antibody (anti-HIV) and hepatitis C antibody (anti-HCV) (and for Treponemal antibodies as a marker of syphilis infection). Donations with any of these markers detected by the testing performed were excluded from the blood supply. Even in the presence of such testing, several circumstances could lead to HBV, HCV or HIV infectious donations entering the blood supply:

1. *Sero-negative infectious donations.* A period of sero-negativity - the 'window period' - prior to detectable levels of antibody or antigen, follows infection with HBV, HIV or HCV. During acute, resolving, HBV infection there is a second HBsAg negative, infectious window, following the transient presence of detectable HBsAg in the blood. During the tail end of HBV carriage HBsAg may fall below detectable levels for a considerable period of time before HBV infectivity is lost (Hoofnagle, 1986). HBsAg testing cannot therefore be assumed to detect all established HBV infections and the risk of HBV infectious donations collected from sero-negative infectious donors during the tail end of HBV carriage should be included to give an overall risk estimate.

Although some patients have been described with HIV infection, and some with HCV infection, who have no antibodies to these infections, such cases are, so far, restricted to immunosuppressed individuals (e.g.Durand F, 2000). For this analysis, it has been assumed that HIV and HCV infections, once established in immunocompetent individuals, result in persistent antibody presence and therefore can always be detected by antibody testing, and that individuals who are known to be immunosuppressed, or have characteristics that suggest they are likely to be immunosuppressed, are excluded from donating blood.

2. *False negative test results.* Tests for HBsAg, anti-HIV and anti-HCV are never 100% sensitive and some positive samples will give false negative results. The high sensitivity of the tests chosen for blood donation testing, and the low prevalence of these markers in UK donations, result in a very high positive predictive value for a negative test result. As large numbers of donations are tested however, the low risk of a false negative should not be assumed to be negligible. The sensitivity of tests to infections in donors may alter if sub-types, or mutant strains, of infections that were not included during the tests' evaluations become more prevalent in the donor population. Sub-types and mutants do occur and can result in alarms about transfusion safety. The relative contribution of different test sensitivities to the overall risk of

infectious donations entering the blood supply is therefore of interest and should be monitored.

3. *Laboratory error.* Laboratory errors can result in a positive sample being credited with a negative result - either due to an error in sampling or conducting the test, or due to an error in recording test results. Controls on every part of the testing process and the information technology involved in recording results aim to prevent such errors occurring and going unnoticed. However, these may not always work, or may not prevent an unforeseen circumstance leading to the release of a positive donation, and the risk resulting from errors should be considered.

In this chapter, data from infection surveillance databases and from special surveys are used, along with estimates of the sensitivity and window periods of current tests, and the estimated rate of error in the testing process, to estimate the risk of HBV, HIV and HCV infectious blood donations entering the blood supply issued to hospitals from English blood centres between 1993 and 1998.

5.2 Methods

Study population

Information about all donations tested during six years, 1993 to 1998, at all blood centres in England (15 at the beginning of the period, reducing to 10 by the end of the period) was included in the study.

Donations were sub-classified into donations from new donors and donations from repeat donors. A repeat donor was a donor who had a recorded attendance as a donor previously. A new donor was a donor who had not attended previously according to that blood centre's current records, although, in some cases, such donors may have attended many years ago, or at another blood centre previously. A positive donation from a repeat donor did not always represent a seroconversion since the last attendance for three reasons. Firstly, not all repeat donors who have attended a donor session previously had given a donation (for example, if they failed haemoglobin tests) and been tested for all infections previously. Secondly, repeat donors who have had a marker of

infection detected by the blood service in the past, and been asked not to donate again, do occasionally re-donate (7% of positive donations from previously tested donors between 1/10/95 and 31/12/98 were from previously confirmed positive donors). Thirdly, as new tests are introduced into donation testing and the sensitivity of tests improve, donors who have not been tested previously or who were negative to previous test kits may be found to be positive (32% of positive donations from previously tested donors between 1/10/95 and 31/12/98 were from donors who had not been previously tested for the infection detected). Details about the testing of previous donations from positive donors were therefore sought so that they could be accurately classified as first-time tested donors and previously tested donors. Previously tested donors were sub-classified as donors who had seroconverted and donors who were, or may have been, seropositive at the time of the previous test and could not be shown to have seroconverted. It was not possible to similarly classify the total numbers of all donations tested from repeat donors into those from first time tested donors and those from previously tested donors. A portion of the denominator used in the incidence estimates may therefore not have been previously tested for anti-HCV and this may dilute the HCV incidence estimate a little. However a study at one blood centre of donations tested during 1993 found that only 1.8% of all donations from repeat donors had not been previously tested for HCV (Atrah, 1996): the effect on the results of such a small, and diminishing, amount of misclassification in the denominator is negligible and no adjustment to compensate for this was made.

Collection of data needed to estimate the risk of infectious donations entering the blood supply

Prevalence of HBsAg, anti-HCV and anti-HIV in new and repeat donors

The numbers of HBsAg, anti-HIV and anti-HCV seropositive donations from new and repeat donors and the numbers of donations tested from new and repeat donors during each year were obtained from surveillance databases and special surveys of HBsAg positive donations and anti-HCV positive donations and used to calculate the prevalence of each infection within donations from new and from repeat donors.

Incidence of HBsAg, anti-HCV and anti-HIV in new and repeat donors

Incidence rates in repeat donors were derived from observed seroconversions. Repeat donors who had seroconverted for anti-HIV were identified from surveillance reports to the NBS and to the Public Health Laboratory Communicable Disease Surveillance Centre (PHLS-CDSC) AIDS/HIV Centre. Repeat donors who had seroconverted for anti-HCV were identified by a retrospective survey of blood centre records (Soldan, 1998) prior to October 1995 and from the NBA/PHLS CDSC surveillance system from October 1995 to the end of 1998. The results of screening and confirmatory tests performed on the last negative, and the first positive, donation were reviewed for all cases of putative anti-HCV seroconversion. Cases with possible but not proven seroconversion, e.g. due to test batch variation, or unsupported interpretations of indeterminate test results were classified as probable false seroconversions, and were not included as seroconverters. The results of HBsAg tests on any previous donations from the donors of HBsAg positive donations were also collected either directly from blood centres or from reports to the infected donor surveillance and repeat donors who had seroconverted for HBsAg were identified. The criteria used to identify a seroconverter from their test results are shown in Table 5.1. A seroconverter was defined as a donor who had made a seropositive donation during the study period (1993-98) and had made a seronegative donation within the ten years prior to the positive donation. Some other similar studies conducted in other countries have classified as seroconverters only those donors whose positive donation and previous negative donation fell within the study period. This method of defining seroconverters within a study reduces the number of seroconverters, but, as the inter-donation interval for the excluded seroconverters is very long, the contribution these make to the risk of a window period donation may be negligible. To investigate the effect of only including seroconverters whose negative donation was within the study period, this approach was also tried and the resulting incidence rate estimates, and risk estimates, were compared. Incidence rates in repeat donors were calculated as the number of seroconverting donors divided by the total number of person years at risk. The number of person years at risk was calculated as the number

of donations made by repeat donors multiplied by an estimate of the average interval (in years) between donations from repeat donors (see below).

Table 5.1 Criteria for defining seroconverters from donation testing results.

Pre-seroconversion donation		Post-seroconversion donation		
HCV				
1. RIBA 3.0 non-reactive	and	RIBA 3.0 positive		
or				
2. ELISA non-reactive & RIBA 2.0 non-reactive	and	ELISA (of same manufacturer and generation as pre-seroconversion test) positive & RIBA 2.0 positive	and	not PCR negative **if** < 12 months after pre-seroconversion donation
or				
3. ELISA 3.0 non-reactive	and	ELISA 3.0 positive & RIBA positive		
HBV				
1. Negative for HBsAg by EIA, or RIA	and	Positive for HBsAg by EIA or by RIA, confirmed by positivity for other HBV marker(s).	and	No evidence of false negative results pre-seroconversion
HIV				
1. Negative for anti-HIV by EIA	and	Positive for anti-HIV by EIA confirmed by alternative EIAs and positivity to Western Blot or PCR.		No evidence of false negative results pre-seroconversion

Incidence was estimated using seroconversions after a negative donation within the previous ten years and for the more recent three-year study period, after a negative donation within that three-year study period.

Because donors who seroconvert may have shorter or longer inter-donation intervals between their pre-seroconversion donation and their post-seroconversion donation than the majority of donors, the probability of a window period donation may actually be greater or less than the average probability that is calculated by the method described below (see "Probability of bleeding an infectious window period donation", page 178). For example, if infected donors

had inter-donation intervals 3 times the length of ordinary inter-donation intervals, the chance of the final day of their inter-donation interval being during a randomly falling window period of X days during their inter-donation interval would be 1/3 the chance of the final day of a non-seroconverting donor's inter-donation interval being during a randomly falling period of X days during their inter-donation interval. The probability of a window period donation as calculated above was therefore multiplied by an adjustment factor S.

$$S = \frac{\text{inter-donation interval for non-seroconverting donors}}{\text{inter-donation interval for seroconverting donors}}$$

S was calculated for each infection using the mean inter-donation interval for non-seroconverting donors and the median inter-donation interval observed for seroconverters detected during the years 1996-98.

S_{HIV} = 315/514 = 0.61 (NB.mean interval for seroconverters =709, St dev =704)

S_{HCV} = 315/419 = 0.75 (NB.mean interval for seroconverters =577, St dev =407)

This adjustment was not applied to the calculations for HBV risk because, as explained on page 171, the inter-donation intervals of detected HBsAg seroconverters were biased towards shorter intervals due to the transient nature of HBsAg.

S_{HBsAg} (not used)= 315/154 = 2.05 (NB. mean interval for seroconverters = 175, St dev = 72)

If it is assumed that the detected HBsAg seroconverters are the lower ranking of all the (inferred) HBV incident donors with respect to inter-donation intervals, they occupy the bottom 37 % of inter-donation intervals. The mean inter-donation interval of the bottom ranking 37% of the anti-HIV and anti-HCV seroconverters (ranked by inter-donation interval) was 227 days. This artificially biased inter-donation interval for the HIV and HCV infected donors is much closer (1.3 times) to that observed for the biased sample of HBV infected donors, than the average for all HIV and HCV seroconverters (662 days - giving an interval 3.8 times the HBV sample). The assumption was therefore made that the total (63% unobserved) group of HBV infected repeat donors had a similar distribution of inter-donation intervals to HIV and HCV infected repeat

donors and that the value of S most appropriate for the HBV estimates was therefore calculated using the average for all anti-HIV and anti-HCV seroconverters.

$S_{HBV} = 315/478 = 0.66$ (NB. mean interval = 662, St dev = 613)

For the years for which seroconversions were identified from Infected Donor reports, and there was some underreporting, the numbers of seroconversions for each infection and for each year were adjusted for underreporting by multiplying the identified numbers by 1/the proportion of all infections in repeat donors that were reported during that year.

HBsAg adjustment

HBsAg is generally transient in individuals infected with HBV as adults and the HBsAg test will have reverted to being negative in many HBV infected donors by the time of their next donation. All the long term HBsAg testing of donations will identify carriers and only some of the donors with transient antigenaemia. The probability of detection of an incident infection by subsequent HBsAg testing therefore had to be calculated.

Other workers, including Korelitz et al (1997), have published estimates of HBV incidence using a method that takes transient antigenaemia into account by calculating the weighted probability that donation testing would detect seroconversion. Korelitz et al assumed that 70% of infected donors would have transient antigenaemia lasting an average of 63 days (the mid point of two published estimates, (Hoofnagle, 1978; Mimms, 1993)), that 25% of infected donors would have no antigenaemia and that 5% would have persistent antigenaemia.

In this study it was similarly assumed that 5% of donors would have persistent antigenaemia. For the remaining 95% of infections it was assumed that 85% would have typical transient antigenaemia lasting an average of 63 days and that 10% would have a heightened and more rapid clearance of antigen lasting just 30 days (Hoofnagle, 1986).

The chance that an incident HBV-infected donor would be detected by HBsAg testing was therefore:

Probability of detection as HBsAg seroconverter = (5%x1)+(85%xT_1)+(10%xT_2)

where,

T_1 = probability that a donor with typical transient antigenaemia is HBsAg positive at time of donation, and

T_2 = probability that a donor with rapid transient antigenaemia is HBsAg positive at time of donation

with,

$$T = \frac{\text{duration of antigenaemia}}{\text{Inter-donation interval}}$$

The average inter-donation interval for the 20 HBsAg seroconverting donors detected during 1996-1998 was 175 days (St dev 72). So,

T_1 = 63/175 = 0.36

T_2 = 30/175 = 0.17

and

Probability of detection as HBsAg seroconverter = (5% x 1) + (85% x 0.36) + (10% x 0.17)

= 0.373, or 37%

The observed HBsAg incidence rate was therefore multiplied by 1/0.373 = 2.68 to give an estimate of the total HBV incidence rate.

New donor risk factor estimation

The incidence of HIV and HCV in new donors cannot be measured directly from current routine test results (specialised testing such as anti-HCV avidity testing and de-tuned anti-HIV testing offer potential for direct identification of recent infections). An adjustment figure (Z) was calculated to represent the difference in incidence between new donors and old donors. This was applied to the incidence rates in repeat donors to produce an estimate of the incidence rates in new donors i.e. incidence in new donors = incidence in repeat donors x Z. Several methods were used to estimate Z.

New donor incidence multiplier method 1: The ratio of the frequency of acute HBV in donations from new donors to the frequency of acute HBV in donations from repeat donors was used to derive Z.

$$Z_1 = \frac{\text{Acute HBV donations per 100,000 donations from new donors}}{\text{Acute HBV donations per 100,000 donations from repeat donors}}$$

Using data from North London Blood Centre, 1993-1998 where 7 acute HBV donations were collected amongst 215,366 donations from new donors and 9 acute HBV donations were collected amongst 1,251,411 donations from repeat donors, Z was estimated as shown below.

$$Z_1 = \frac{7/2.15366}{9/12.51411} = \frac{3.25}{0.72} = 4.51$$

New donor incidence multiplier method 2: A method used in a study by Lackritz *et al* (1995) was used. This method is based on the understanding that at the start of testing, when no repeat donors have been excluded because of a positive test result, the seroprevalance of a persistent marker of infection is equivalent to the cumulative incidence of the infection. If the time at risk of infection has been the same for new donors and repeat donors, the ratio of the seroprevalence in new donors and repeat donors during the first period of testing can be used as an estimate of Z. The period of time used should not contain any repeat tests on the same individual. Lackritz *et al* took the first year of testing. As donors can donate up to 3 times each year (every 16 weeks), and some repeat donors do donate more than once a year, the ratio for each calendar quarter during the first 15 months of testing was calculated to check the period of testing used for calculating Z did not include any quarter that showed a ratio that may have been inflated by inclusion of negative repeat donors in the denominator for the repeat donor prevalence (see table 5.2). The prevalence of anti-HIV amongst new donors during the first year of testing (Oct-85-Sep-86) was 5.15 times that amongst repeat donors. During the first six months and second six months of testing the prevalence in new donors was 3.67 times that amongst repeat donors, and 6.08 times that amongst repeat donors respectively. The prevalence in new donors in 1997 was 6.73 times the prevalence in repeat donors, and has remained at around this level since (ratio for 1987 to 1997 = 8.43). Z_2 was therefore taken as the ratio for the first six months as by the second six month period the ratio had increased towards the ratio observed once repeat donors with prevalent infections had been excluded from the donor panel. It was assumed that when HIV testing was introduced all donors had been at risk of HIV infection for 6 years, since 1980.

$$Z_{2(HIV)} = \frac{\text{Anti-HIV prevalence in new donors during 1st 6 months of testing}}{\text{Anti-HIV prevalence in repeat donors during 1st six months of testing}}$$

$$Z_{2(HIV)} = 3.67$$

Table 5.2 HIV prevalence during first 15 months of anti-HIV testing of blood donations.

Time period	Total tested donations	New donations	Donations from repeat donors	Total HIV positives	New donor HIV positives	Repeat donor HIV positives	Prevalence per 10,000 repeat donor donations	Prevalence per 10,000 new donor donations	Ratio of new donor to repeat donor prevalence
Q1 (Oct-Dec'85)	527969	63356	464613	8	3	5	0.11	0.47	4.40
Q2 (Jan-Mar'86)	565299	67836	497463	10	3	7	0.14	0.44	3.14
Q3 (Apr-Jun'86)	560966	73914	487052	12	6	6	0.12	0.81	6.59
Q4 (Jul-Sep'86)	558289	67856	490433	20	9	11	0.22	1.33	5.91
Q5 (Oct-Dec'86)	561962	77642	484320	27	11	16	0.33	1.42	4.29
Q1-Q2	1093268	131192	962076	18	6	12	0.12	0.46	3.67
Q3-Q4	1119255	141770	977485	32	15	17	0.17	1.06	6.08
Q1-Q4	2212523	272962	1939561	50	21	29	0.15	0.77	5.15
Q2-Q5 (86)	2246516	287248	1959268	69	29	40	0.20	1.01	4.95
Q1-Q5	2774485	350604	2423881	77	32	45	0.19	0.91	4.92
1987	2223713	287553	1936160	12	6	6	0.03	0.21	6.73
1987-1997	27022326	3380026	23642300	236	129	107	0.05	0.38	8.43

Data about anti-HCV positive donations per month were not available for the first year of anti-HCV testing (September 1991 to August 1992). The prevalence of anti-HCV amongst new donors during the first full year of testing (1992) was 4.05 times that amongst repeat donors. Adjusting this ratio by the increase observed in the anti-HIV data between the first six month's ratio and the first year's ratio resulted in an estimate of the ratio for the first six months for anti-HCV of 2.88 (=4.05 x (3.67/5.15)).

It was assumed that when HCV testing was introduced all donors had been at risk of HCV infection since the age of 15 years. Repeat donors have an average age of approximately 42 years and new donors have an average age of approximately 33 years. The new donor incidence multiplier for anti-HCV was therefore estimated as the estimated prevalence ratio for the first six months of 1992 multiplied by the difference in the time at risk for new donors and repeat donors.

$$Z_{2(HCV)} = \frac{\text{Prev new dons 1992}}{\text{Prev repeat dons 1992}} \times \frac{\text{Ratio for HIV 1st 6mo}}{\text{Ratio for HIV 1st 12 mo}} \times \frac{\text{Repeat dons yrs at risk}}{\text{New dons yrs at risk}}$$

$$Z_{2(HCV)} = 4.05 \times 0.71 \times 1.5 = 4.32$$

New donor incidence multiplier method 3: A third method was adapted from Cumming *et al.* Cumming *et al* estimated incidence by using the time at risk to convert prevalence rates (the results of cumulative incidence) to annual incidence rates. Half the total time since the beginning of HIV infection spread and the present time was used as a measure of time at risk for new (and previously untested) donors. Cummings *et al* (1989) proposed using half the total time in order to compensate for the increasing, and non-linear, risk of HIV infection over this time. We applied this method to 1993-1998 prevalence data for repeat donors and new donors in England, assuming HIV infection spread began in England in 1980, that new donors had been at risk of HCV infection since the age of 15, and that new donors had been at risk of HBV infection since birth. Z_3 was then estimated by dividing the annual incidence rate for new donors by the annual incidence rate for repeat donors. For HCV - an infection with a relatively high prevalence in repeat donors - the comparable "annual incidence" for repeat donors was the sum of the incidence calculated from seroconversions and annual incidence calculated from prevalence as for new donors.

$$Z_{3HIV} = \frac{\text{annual incidence new donors}}{\text{annual incidence repeat donors (as in Table 5.5)}} = 1.82$$

where,

$$\text{Annual incidence new donors} = \frac{\text{prevalence during 1993-1998}}{\text{average annual time at risk}}$$

$$= 0.69/100{,}000\text{pys}$$

with,

$$\text{Average annual time at risk} = \frac{\text{(Sum of (each year in study-1980)/6)}}{2}$$

$$= 7.8\text{yrs}$$

and

$$Z_{3HCV} = \frac{\text{annual incidence new donors}}{\text{annual incidence repeat donors}} = 7.68$$

where,

$$\text{Annual incidence new donors} = \frac{\text{prevalence during 1993-1998}}{\text{average annual time at risk}}$$

= 3.92/100,000pys

with,

Average annual time at risk = (average age – age first at risk)

= (33-15) = 18yrs

and ,

Incidence repeat donors =

Incidence of seroconversion + $\frac{\text{prevalence during 1993-1998}}{\text{average annual time at risk}}$

= 0.26 [from Table 5.5] + 0.25 = 0.51/100,000pys

and

Z_{3HBV} = $\frac{\text{annual incidence new donors}}{\text{annual incidence repeat donors (as in Table 5.5)}}$

= 2.70

where,

Annual incidence new donors = $\frac{\text{prevalence during 1993-1998}}{\text{average annual time at risk}}$

= 1.1/100,000pys

with,

Average annual time at risk = (average age – age first at risk)

= (33-0) = 33

New donor incidence multiplier method 4: A fourth method of estimating Z was adapted from Dax *et al* (1992). This method used prevalence data and probability of donating during the seronegative window period stage of infection (i.e the seronegative window period as a proportion of the total time course of infection for new donors, and the seronegative window period as a proportion of the inter-donation interval for repeat donors). Dax *et al* assumed that the number of first-time donors who donate whilst in the window period is the product of the proportion of the time course of infection during which the tested marker is not present and the prevalence of the marker in new donors, and that the number of repeat donors who donate whilst in the window period is the product of the proportion of the inter-donation interval during which the tested marker is not present and the prevalence of the marker in repeat tested donors. Z_4 was estimated as the ratio of these numbers. Again, because of the high

prevalence in repeat donors (due to accumulated past incidence), the comparable calculation for repeat donors included incidence derived from prevalence.

$$Z_4 = \frac{\text{window period donations new donors}}{\text{window period donations repeat donors}}$$

with, for HIV

Window period donations new donors = (22/(10 x 365)) x (89/1,662,238) = 0.032/100,000

WP donations repeat donors = (22/(45 x 7)) x (42/12,939,000)
= 0.023/100,000

Z_{4HIV} = 1.39

with, for HCV

WP donations new donors = (66/(25 x 365)) x (1,172/1,662,238)
= 0.51/100,000

WP donations repeat donors = ((66/(45 x 7)) x (29/12,939,000)) + ((66/(25 x 365)) x (570/12,938,971)) = 0.047 + 0.032 = 0.079/100,000

Z_{4HCV} = 6.46

with, for HBV

WP donations new donors = (110/(25 x 365)) x (607/1,662,238)
= 0.44/100,000

WP donations repeat donors = (110/(45 x 7)) x (46/12,939,000)
= 0.12/100,000

Z_{4HBV} = 3.67

Table 5.3 summarises the estimates of Z obtained from applying these methods to English data. The value of Z used for our "standard" estimates was the mean value for each infection.

Table 5.3 Values of new donor window period risk multiplier (Z)

	HBV	***HCV***	***HIV***
Method 1: Direct observation of acute infections	4.51	NA	NA
Method 2: Cumulative incidence at start of testing	NA	4.32	3.67
Method 3: Incidence from prevalence and time at risk.	2.70	7.68	1.82
Method 4: Prevalence and WP as proportion of total infection course	3.67	6.46	1.39
Mean (all available methods)	***3.63***	***6.15***	***2.29***

The overall incidence rate of an infection was calculated as the weighted average of the incidence rates in new and repeat donors.

Inter-donation intervals

The average inter-donation interval estimates was derived from data provided from one blood centre for the three-year period 1993-1995. 606,193 donations were collected from 173,777 repeat donors, giving 3.49 donations per donor over 3 years, or 3.39/3 = 1.16 donation per year. The average inter-donation interval was estimated as 365/1.16 = 314 days or 45 weeks (0.86 years).

The inter-donation interval for the seroconverters was calculated directly from the dates of the last negative and first positive donation.

Estimation of risk of infectious donations entering the blood supply

Probability of bleeding an infectious window period donation

The probability of a seronegative donation being made during the window period was calculated firstly (WP method 1) as equal to the incidence of infection in donors, multiplied by estimates of the infectious window periods during acute infection.

$$\text{WP risk}_1 = \text{incidence x window period}$$

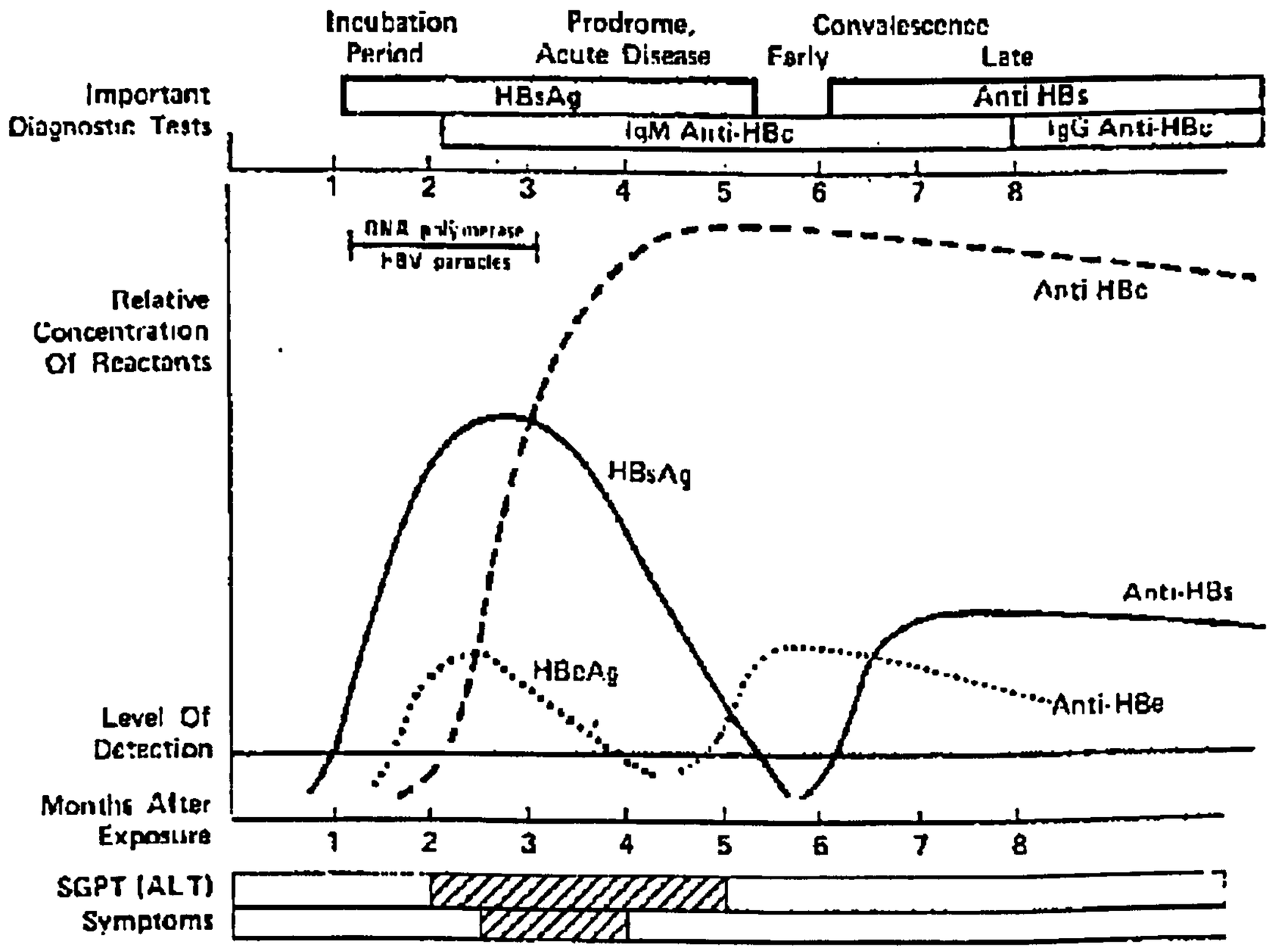
Tests used during the study period detect anti-HIV and anti-HCV 22 days (Busch, 1995) and 66 days (Barrera, 1995) after HIV and HCV infection respectively. The upper and lower values of these window periods were 6 days and 38 days for anti-HIV and 54 days and 192 days for anti-HCV.

The patterns of infectivity and serological markers for HBV are slightly more complex. Figure 5.1 shows the patterns of serological markers during acute, resolving infection. Three windows during which infectious blood could be collected were considered: the "early acute window" after exposure and prior to any serological markers, the "late acute window" of resolving infection when HBsAg is below detectable levels but anti-HBs is not present and some infectivity remains, and the "tail-end window" at the end of HBsAg carriage when HBsAg falls below detectable levels in advance of total loss of infectivity.

Current tests detect HBsAg a median of 59 days after HBV infection, with upper and lower values of 37 days and 87 days respectively (Mimms, 1993).

Figure 5.1 Serological and clinical patterns observed during acute HBV infection.

(From Manual of Clinical Microbiology, Lennete, Balows, Hausler and Shadomy)



The period between loss of HBsAg and loss of infectivity during resolving acute infections - the late acute window - was estimated to be another 30 days (range 10 to 50). The average effective total window period during acute infection was calculated as the early acute window for all infections plus the late-acute window for 95% of infections expected to resolve and therefore to pass through this late acute window.

Total HBV acute window = 59 + (0.95 x 30) = 87.5 days

With lower and upper values of 46.5 days (37 + (0.95 x 10) and 134.5 days ((87 + (0.95 x 50).

Donations bled immediately after a donor has been infected are unlikely to contain enough viruses to be infectious. This period immediately after infection when nucleic acids cannot be recovered from the blood is often called the "eclipse" period, and results in the infectious window period being shorter then the total window period from infection to positive serological markers. It is thought likely that this eclipse period is proportional in length to the total window period, however, for simplicity and in the absence of specific data a 7-day non-infectious period immediately after infection was taken for each virus. The antibody/antigen window period estimates, and the lower value for these estimates, were therefore decreased by seven days to give an infectious window period.

Upper and lower limits to the risk estimates were calculated using the extremities of the ranges of the incidence rate estimates, and of the ranges of the window periods. 95% credibility intervals for the risk estimates were calculated by simulation to reflect the sampling variability of the incidence and prevalence estimates and uncertainty about the infectious window period. This was done by using Poisson distributions with observed rates for the number of seroconversions and the prevalence numerators, and a triangular distribution for the infectious window period. The inter-donation interval, proportion of donations from new donors, time at risk adjustment factor and number of donors tested during the first year of testing were kept constant.

An alternative approach to estimating the risk of a window period (WP method 2) was also used. This approach did not work from incidence, but by

summing the probability of previous donations from seroconverting donors having been made during the window period.

$$\text{WP risk}_2 = \frac{\text{number of SC x (WP/median pre-SC donation interval)}}{\text{number of repeat donor donations}}$$

This method has been used by Gluck, 1998 and Muller-Breitzeutz, 2000. This method has the advantage of directly accommodating the effect of longer inter-donation intervals in donors who seroconvert than in other donors.

Probability of test failure or error

The risk of a seropositive donation not being identified by testing was equal to the probability of false negative test result estimated using the sensitivity of the test and the prevalence of the marker.

$$\text{FN risk} = \frac{\text{(prevalence) x (1-sensitivity)}}{\text{sensitivity}}$$

Upper and lower limits on the risk were calculated using the upper and lower 95% confidence intervals for the prevalence rate. The sensitivity of anti-HCV tests was 99% (PHLS, 1995) and the sensitivity of anti-HIV tests was 99.5%. The sensitivity of HBsAg tests was assumed to be 1.

Process error was defined as any technical or human error in the testing, recording, or discarding of infectious donations. The error rate was estimated to be 0.5%, based on data from USA (Linden, 1994 a&b). No published rates of technical or human errors in the testing, recording, or discarding of donations in the UK were available. There is evidence that errors do still occur in England: one case of transfusion transmitted HCV by an anti-HCV positive donation released by an error in the testing process has been documented (see Chapter 3) and two incidents of HCV testing failures allowing donations from HCV infected donors to be released (neither resulting in infection of a recipient) have been reported. The risk of a Process Error involving an infectious donation was equal to the estimated probability of a Process Error (0.5%) multiplied by the probability of a donation being seropositive.

$$\text{PE risk} = \text{prevalence x error rate}$$

Probability of HBsAg negative donations during tail-end carriage

The frequency and duration of HBsAg negative, infectious, periods at the tail end of HBV carriage in blood donors was not known. The relative frequency of observed transfusion transmitted HBV by these two causes was used to scale-up the estimates of risk due to donations from acute donors to the overall risk due to donations from acute donors and donations from tail-end carriers. A review of all cases of reported acute HBV infection associated with transfusion in England and Wales between 1991 and 1997 (Soldan, 1999) found 11 of 14 (79%) cases were due to donations from donors with HBV carriage and 3 were due to donations from donors with acute HBV infection (none were due to errors) (see Chapter 4). A similar observation has been made by North London blood centre where 10 of 13 (77%) cases between 1985 and 1993 were due to donations from donor bled during the infectious, but HBsAg negative, period at the tail-end of HBsAg carriage (Barbara, personal communication). The risk of infectious donations from tail-end carriers was therefore estimated by multiplying the risk of window period donations by 11/3 = 3.67. The upper and lower limits for this estimate were calculated using the upper and lower limits of the window period risk and the upper and lower limits of the 95% confidence interval of the proportion of observed transmission due to carriers.

Sensitivity analysis

The effect of uncertainty in the data and assumptions used in the estimations was investigated by varying the parameters used and recording the absolute and percentage change in the resulting estimates. Two groups of variations were considered.

Firstly, variations were made in the parameters (usually derived from other data and assumptions) that were used for which there was little supporting evidence, and therefore may have been incorrect. Several parameters in this category were varied. The accuracy with which incidence can be derived from observations of reported seroconversions in repeat donors can be questioned (as discussed in chapter 4). In order for a new infection to be detected the donor has to donate once before infection and once after infection. Further more, the criteria used to define a seroconversion were designed to exclude the

relatively large numbers of "apparent" seroconversions, and the requirement for documented proof of a change from negative to positive, comparable, serology, may have excluded some true seroconversions as well as many "apparent" seroconversions. The number of seroconversions is therefore likely to be an underestimate of the true number of new infections in the person years observed. A 50% and a 100% increase in the numbers of new infections entering the incidence calculations was used in the sensitivity analyses to investigate the effect on the resulting risk estimates of a higher incidence rate. Another source of possible error in the incidence estimates was the derivation - rather than observation - of the person years at risk. The mean inter-donation interval was used, but the estimate of the mean may have been wrong, and the use of the mean rather than the median may also have resulted in error in the incidence rate denominator. A 20% increase and decrease in the person years at risk entered into the incidence calculations was used in the sensitivity analyses to investigate the effect on the resulting risk estimates of a varied true number of person years at risk. The new donor multiplier was a very uncertain parameter. The upper and lower estimates of the new donor multiplier obtained from the various methods described earlier was used in the sensitivity analyses to investigate the effect on the resulting risk estimates of the uncertainty in this parameter. The rate of errors in blood centres that would allow the release of positive donations is not well known. Errors are known to have occurred and the rate used in the best estimates was in line with published rates and observations within the blood service. However, this is contentious and the rate could be higher of lower. A 100% increase (i.e. 1 error every 100 donations tested) and decrease (i.e. no errors) in the error rate was used in the sensitivity analyses to investigate the effect on the resulting risk estimates of different error rates.

Secondly, variations were made in parameters that were relatively well known (usually observed), but that may change over time. Several parameters in this category were varied. The prevalence and incidence of infection markers in blood donations may change over time. During the period considered, the prevalence of anti-HCV in blood donations collected in England and Wales was declining (from 17.9 to 6.8 positives per 100,000), the prevalence of anti-HIV was not changing, but did fluctuate from year to year with minimum of 0.7 to a maximum of 1.1, and the prevalence of HBsAg was falling slightly from 5.0 to

4.5 positives per 100,000 donations. The overall incidence of each infection in repeat donors was not obviously changing over this period, but may change in the future depending on the epidemiology of these infections in the donor population and on donor recruitment and selection practices. A 50% rise and fall in prevalence (in all donations) and incidence (in repeat donors) of infection in blood donations was used in the sensitivity analyses to investigate the effect on the resulting risk estimates of changing frequency of infection in the donor population. Eleven percent of donations were collected from new donors over the period studied: this was consistent each year. The proportion of donations collected from new donors may change in the future as donor recruitment and selection practices change to meet the demands for blood. A 50% rise and fall in the proportion of donations collected from new donors (i.e. from 5.5% to 16.5) was used in the sensitivity analyses to investigate the effect on the resulting risk estimates of changing proportions of donations collected from new donors. Serological tests are, in general, expected to continue improving in sensitivity and in the detection of early window period infections. A 20% and 50% reduction in window period, and a 20% and 50% improvement in sensitivity were used in the sensitivity analyses to investigate the effect on the resulting risk estimates of improvements in test performance.

Estimates for the variations described above in each parameter, and for the range of all parameters in each category, and for all parameters in both categories together, were produced.

5.3 Results

Prevalence of infection

During the six-year period 1993-1998, English blood centres tested 14,601,238 donations: 12,939,000 (89%) of these donations were from repeat donors and 1,662,238 (11%) were from new donors. A total of 2,621 (0.02%) donations were found to have confirmed markers of HIV (145, 0.99 per 100,000), HCV (1,771, 12.1 per 100,000) or HBV (705, 4.83 per 100,000) infection.

Table 5.4 shows the prevalence rates of markers of HBV, HCV and HIV infection in blood donations in England, 1993-1998.

Table 5.4 Prevalence of HBsAg, anti-HCV and anti-HIV in blood donations in England 1993-98.

Donation type	*1993-1995*			*1996-1998*			*1993-1998*		
	Tested (1,000s)	***Pos***	***prev. per 100,000***	***Tested (1,000s)***	***Pos***	***prev. per 100,000***	***Tested (1,000s)***	***Pos***	***prev. per 100,000***
HBsAg									
From repeat donors	6,361.9	41	0.64	6,577.1	57	0.87	12,939.0	98	0.76
From new donors	870.2	322	37.00	792.0	285	35.98	1,662.2	607	36.52
All donations	7,232.1	363	5.02	7,369.1	342	4.64	14,601.2	705	4.83
Anti-HCV									
From repeat donors	6,361.9	414	6.51	6,577.1	185	2.81	12,939.0	599	4.63
From new donors	870.2	727	83.54	792.0	445	56.18	1,662.2	1,172	70.51
All donations	7,232.1	1,141	15.78	7,369.1	630	8.55	14,601.2	1,771	12.13
Anti-HIV									
From repeat donors	6,361.9	30	0.47	6,577.1	26	0.40	12,939.0	56	0.43
From new donors	870.2	49	5.63	792.0	40	5.05	1,662.2	89	5.35
All donations	7,232.1	79	1.09	7,369.1	66	0.90	14,601.2	145	0.99

Incidence of infection

Based on data from one blood centre about the number of donors tested during 1993-1995, the average inter-donation interval for repeat donors over that three-year period was estimated to be 45 weeks (average number of donations per year per repeat donor = 1.16).

The new donor incidence adjustments (Z) used were 3.63 for HBV, 6.15 for HCV and 2.29 for HIV.

Table 5.5 shows the incidence rates of seroconversion for HBsAg, anti-HCV and anti-HIV in repeat blood donors in England, 1993-1998.

Table 5.6 shows the estimated incidence in new donors, and the weighted incidence in all donors in England, for the 2 three year periods and the total study period 1993-1998.

Estimates of risk of donations from infected donors entering the blood supply

Tables 5.7a), b) and c) show estimates of the frequency of donation from a) new donors, b) repeat donors and c) all donors with HIV, HBV or HCV infections entering the blood supply for the periods 1993-95, 1996-98 and 1993-98.

Upper and lower limits of the ranges were calculated using the 95% confidence interval for the incidence rates, the range of the length of the window periods during acute infection, the upper and lower limits of the 95% confidence interval for the prevalence rates. Upper and lower limits of the range on the total (combined) risks were calculated using the upper and lower limits of the component risks.

Figure 5.2 shows the proportion of the total calculated risk that was due to each component of risk.

Table 5.5 Incidence of seroconversion for HBsAg, anti-HCV and anti-HIV in repeat donors in England, 1993-98.

	1993-1995			*1996-1998*			*1993-1998*		
	Person years	***No. of sero's***	***incidence per 100,000pys***	***Person years***	***No. of sero's***	***incidence per 100,000pys***	***Person years***	***No. of sero's***	***incidence per 100,000pys***
HBsAg	5,505,515	25	0.4628	5,691,697	20	0.3591	11,197,212	46	0.4101
Anti-HCV	5,505,515	14	0.2543	5,691,697	15	0.2691	11,197,212	29	0.2618
Anti-HIV	5,505,515	15	0.2725	5,691,697	27	0.4744	11,197,212	42	0.3751

Table 5.6 Estimated incidence in new donors, and weighted incidence in all donors.

	1993-1995		*1996-1998*		*1993-1998*	
	incidence in new donors	***incidence in all donors***	***incidence in new donors***	***incidence in all donors***	***incidence in new donors***	***incidence in all donors***
HBsAg	1.2407	1.6333	0.9627	1.2349	0.8590	1.4286
Anti-HCV	1.5639	0.4119	1.6550	0.4181	0.8590	0.4153
Anti-HIV	0.6239	0.3147	1.0863	0.5401	0.8590	0.4302

Table 5.7a) Estimates of the frequency of donations from NEW donors with HIV, HBV or HCV infections entering the blood supply (1993-1998).

	1993-1995	1996-1998	1993-1998
a) HBV			
Risk of donation from infected donor per 100,000 donations:			
- due to window periods of acute infection	0.655	0.508	0.581
95% credibility interval	0.413 - 1.050	0.300 - 0.836	0.421 - 0.892
- due to test error	0.000	0.000	0.000
- due to process error	0.185	0.180	0.183
Range	0.165 - 0.205	0.159 - 0.201	0.168 - 0.197
- total	0.840	0.688	0.763
Range	0.578 - 1.255	0.459 - 1.037	0.589 - 1.089
- estimated number of HBV infected donations	7	5	13
Range	5 - 11	4 - 8	10 - 18
b) HCV			
Risk of donation from infected donor per 100,000 donations:			
- due to window periods of acute infection	0.189	0.201	0.195
95% credibility interval	0.131 - 0.658	0.137 - 0.677	0.159 - 0.623
- due to test error	0.844	0.568	0.712
Range	0.783 - 0.905	0.515 - 0.620	0.672 - 0.753
- due to process error	0.418	0.281	0.353
Range	0.388 - 0.448	0.255 - 0.307	0.333 - 0.373
- total	1.451	1.049	1.260
Range	1.301 - 2.011	0.907 - 1.604	1.163 - 1.748
- estimated number of HCV infected donations	13	8	21
Range	11-18	7 - 13	19 - 29
c) HIV			
Risk of donation from infected donor per 100,000 donations:			
- due to window periods of acute infection	0.016	0.027	0.022
95% credibility interval	0.0073 - 0.0419	0.0141 - 0.0686	0.0117 - 0.0527
- due to test error	0.028	0.025	0.027
Range	0.020 - 0.036	0.018 - 0.033	0.021 - 0.033
- due to process error	0.028	0.025	0.027
Range	0.020 - 0.036	0.018 - 0.033	0.021 - 0.032
- total	0.072	0.078	0.075
Range	0.048 - 0.114	0.049 - 0.119	0.0542 - 0.118
- estimated number of HIV infected donations	1	1	1
Range	0.4 - 1.0	0.4 - 0.9	0.9 - 2.0

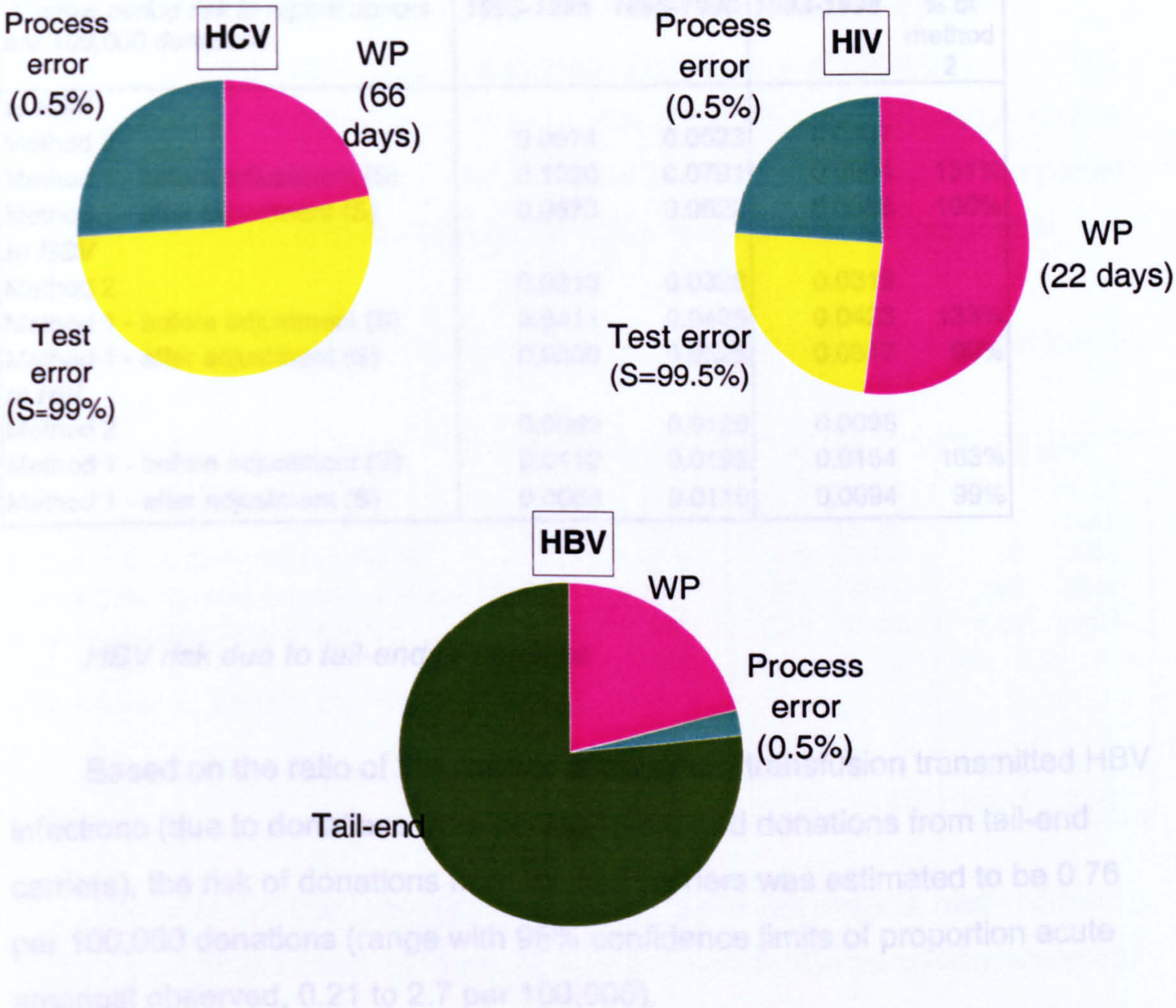
Table 5.7b) Estimates of the frequency of donations from REPEAT donors with HIV, HBV or HCV infections entering the blood supply (1993-1998).

	1993-1995	1996-1998	1993-1998
a) HBV			
Risk of donation from infected donor per 100,000 donations:			
- due to window periods of acute infection	0.180	0.140	0.160
95% credibility interval	0.114 - 0.289	0.083 - 0.230	0.116 - 0.246
- due to test error	0.000	0.000	0.000
- due to process error	0.003	0.004	0.004
range	0.002 - 0.004	0.003 - 0.006	0.003 - 0.005
- total	0.184	0.144	0.164
range	0.116 - 0.293	0.086 - 0.236	0.119 - 0.251
- estimated number of donations	12	9	21
range	7 - 19	6 - 15	15 - 32
b) HCV			
Risk of donation from infected donor per 100,000 donations:			
- due to window periods of acute infection	0.031	0.033	0.032
95% credibility interval	0.021 - 0.107	0.022 - 0.110	0.026 - 0.101
- due to test error	0.066	0.028	0.047
range	0.059 - 0.072	0.024 - 0.033	0.043 - 0.051
- due to process error	0.033	0.014	0.023
range	0.029 - 0.036	0.012 - 0.016	0.021 - 0.025
- total	0.129	0.075	0.102
range	0.110 - 0.215	0.058 - 0.159	0.090 - 0.177
- estimated number of donations	8	5	13
range	7 - 14	4 - 10	12 - 23
c) HIV			
Risk of donation from infected donor per 100,000 donations:			
- due to window periods of acute infection	0.007	0.012	0.009
95% credibility interval	0.0032 - 0.0183	0.0061 - 0.0299	0.0051 - 0.0230
- due to test error	0.002	0.002	0.002
range	0.0015 - 0.0032	0.0012 - 0.0028	0.0016 - 0.0028
- due to process error	0.002	0.002	0.002
range	0.0015 - 0.0032	0.0012 - 0.0028	0.0016 - 0.0028
- total	0.012	0.016	0.014
range	0.006 - 0.025	0.009 - 0.036	0.008 - 0.029
- estimated number of donations	1	1	2
range	0.4 - 1.6	0.6 - 2.3	1.1 - 3.7

Table 5.7c) Estimates of the frequency of donations from ALL donors with HIV, HBV or HCV infections entering the blood supply (1993-1998).

	1993-1995	1996-1998	1993-1998
a) HBV			
Risk of donation from infected donor per 100,000 donations:			
- due to window periods of acute infection	0.235	0.182	0.208
95% credibility interval	0.150 - 0.380	0.109 - 0.303	0.153 - 0.323
- due to test error	0.000	0.000	0.000
- due to process error	0.024	0.024	0.024
range	0.023 - 0.028	0.021 - 0.026	0.022 - 0.026
- due to tail end carriers	0.860	0.667	0.762
range	0.581 - 7.547	0.160 - 2.079	0.208 - 2.701
- total	1.118	0.874	0.994
range	0.753 - 7.954	0.290 - 2.408	0.383 - 3.050
- equivalent to 1 in x donations	89,424	114,480	100,616
range	12,572 - 132,801	41,534 - 345,161	32,784 - 260,960
- estimated number of donations	81	64	145
range	54 - 575	21 - 177	56 - 445
b) HCV			
Risk of donation from infected donor per 100,000 donations:			
- due to window periods of acute infection	0.049	0.052	0.050
95% credibility interval	0.034 - 0.173	0.036 - 0.178	0.042 - 0.164
- due to test error	0.154	0.090	0.123
range	0.151 - 0.169	0.080 - 0.093	0.117 - 0.128
- due to process error	0.076	0.044	0.061
range	0.075 - 0.084	0.039 - 0.046	0.058 - 0.064
- total	0.280	0.186	0.233
range	0.259 - 0.425	0.155 - 0.317	0.217 - 0.356
- equivalent to 1 in x donations	357,688	537,791	428,305
range	235,183-386,100	315,259-645,161	281,057-480,405
- estimated number of donations	20	14	34
range	19 - 31	11 - 23	32 - 52
c) HIV			
Risk of donation from infected donor per 100,000 donations:			
- due to window periods of acute infection	0.008	0.014	0.011
95% credibility interval	0.004 - 0.021	0.007 - 0.035	0.006 - 0.027
- due to test error	0.005	0.005	0.005
range	0.004 - 0.007	0.003 - 0.006	0.004 - 0.006
- due to process error	0.005	0.005	0.005
range	0.004 - 0.007	0.003 - 0.006	0.004 - 0.006
- total	0.018	0.023	0.021
range	0.012 - 0.035	0.014 - 0.046	0.014 - 0.038
- equivalent to 1 in x donations	5,422,019	4,365,928	4,823,425
range (millions)	2.90 - 8.13	2.18 - 7.19	2.62 - 6.99
- estimated number of donations	1	2	3
range	0.9 - 2.5	1.0 - 3.4	2.1 - 5.6

Figure 5.2 Components of the risk of donations from infected donors entering the blood supply.



The results of the alternative window period method (method 2) for the risk of window period donations from repeat donors, along with the comparable results from window period method 1 are shown in table 5.8. The results of the incidence method without adjustment (S), were - as expected - higher than the results of the alternative method. The amount by which they were higher reflected the extent to which the inter-donation intervals of seroconverters were greater than of other donors. After adjustment for this difference, the incidence method estimates were the same as the alternative method's results. It is worth noting that if the mean rather than the median inter-donation intervals for seroconverting donors were used to calculate the adjustment factor S, the results of the incidence method were lower (73%) than the results of the alternative method.

Table 5.8 Results of window period risk estimates method 2.

Window period risk in repeat donors per 100,000 donations	***1993-1995***	***1996-1998***	***1993-1998***	% of method 2
a) HBV				
Method 2	0.0674	0.0523	0.0597	
Method 1 - before adjustment (S)	0.1020	0.0791	0.0904	151%
Method 1 - after adjustment (S)	0.0673	0.0522	0.0596	100%
b) HCV				
Method 2	0.0310	0.0328	0.0319	
Method 1 - before adjustment (S)	0.0411	0.0435	0.0423	133%
Method 1 - after adjustment (S)	0.0308	0.0326	0.0317	99%
c) HIV				
Method 2	0.0069	0.0120	0.0095	
Method 1 - before adjustment (S)	0.0112	0.0195	0.0154	163%
Method 1 - after adjustment (S)	0.0068	0.0119	0.0094	99%

HBV risk due to tail-end of carriage

Based on the ratio of the causes of observed transfusion transmitted HBV infections (due to donations from acute donors and donations from tail-end carriers), the risk of donations from tail end carriers was estimated to be 0.76 per 100,000 donations (range with 95% confidence limits of proportion acute amongst observed, 0.21 to 2.7 per 100,000).

Sensitivity analysis

1. <u>Weakly supported parameters</u>

<u>Identification of seroconverters for incidence estimates</u>

If seroconverters were identified - as in some studies - as positive repeat donors with a previous negative donation during the study period rather than within the past 10 years (as above), the numbers of seroconverters and the length of the inter-donation intervals for seroconverters were reduced. Table 5.9 shows the number of seroconverters, the values for S (adjustment to allow for different inter-donation intervals for seroconverters) and the resulting window period risk estimates and overall risk estimates for the 1996-98 period with the seroconverters identified as positive repeat donors with a negative donation within the study period. For HCV the number of seroconverters was reduced and the median inter-donation interval (and therefore S) changed little: the risk

estimate therefore reduced. For HIV the number of seroconverters reduced by a greater amount and the inter-donation interval also decreased greatly (and S increased) so the resulting risk estimates were reduced more markedly. Estimates for HBV were not re-calculated in this way as detected seroconverters for HBsAg were of short inter-donation intervals (seroconverter detection only affected by 2%, by fall from 4 to 1 for the first year of the period) due to the transient nature of HBsAg and this revision was not applicable.

Table 5.9 Changed criteria (3 year period) for identifying seroconversions for incidence.

	a) HBV[1]		*b) HCV*		*c) HIV*	
		% of "best"		% of "best"		% of "best"
Number of seroconverters 1996-98	17	83%	9	59%	9	33%
Seroconversion inter-donation interval(days)	-	-	371	89%	168	33%
S (seroconverter IDI/average IDI)	-	-	0.78	104%	1.09	179%
Risk of infected donation per 100,000 donations:						
- due to window periods of acute infection	-	-	0.035	67%	0.008	57%
- total	-	-	0.169	91%	0.017	74%

The effect of changes in the numbers of seroconversions, and in other factors that effect incidence rates, was also shown by the sensitivity analyses.

Table 5.10 shows the effects of variations in the parameters used in the risk model for all donations, 1993-98. H = value giving higher risk estimate, L = value giving lower risk estimate.

Table 5.10 Sensitivity analyses results (excluding component of HBV risk due to tail-end carriers).

	HBV					HCV					HIV				
"Best" model:	0.21	0.02	0.23	100%	0.43M	0.05	0.18	0.23	100%	0.43M	0.011	0.010	0.021	100%	4.8
Changes to parameters relatively poorly known:															
New infections	*WP*	*ER*	*TOT*	*% of "best"*	*1 in x*	*WP*	*ER*	*TOT*	*% of "best"*	*1 in x*	*WP*	*ER*	*TOT*	*% of "best"*	*1 in x*
H: x1.5	0.31	0.02	0.34	145%	0.30M	0.08	0.18	0.26	111%	0.39M	0.016	0.010	0.026	126%	3.8M
HH: x2	0.42	0.02	0.44	190%	0.23M	0.10	0.18	0.28	122%	0.35M	0.022	0.010	0.032	152%	3.2M
Pys															
L: x1.2 (13,436,654)	0.17	0.02	0.20	85%	0.51M	0.04	0.18	0.23	96%	0.44M	0.009	0.010	0.019	91%	5.3M
H: x0.8 (8,957,770)	0.26	0.02	0.28	122%	0.35M	0.06	0.18	0.25	105%	0.41M	0.013	0.010	0.023	113%	4.3M
New donor multiplier															
H: upper value of range	0.22	0.02	0.25	107%	0.40M	0.06	0.18	0.24	102%	0.42M	0.012	0.010	0.022	107%	4.5M
L: lower value of range	0.19	0.02	0.22	93%	0.47M	0.04	0.18	0.23	97%	0.44M	0.010	0.010	0.020	95%	5.1M
Error rate															
H: 100% up (0.01)	0.21	0.05	0.26	110%	0.39M	0.05	0.24	0.29	126%	0.34M	0.011	0.015	0.026	124%	3.9M
L: 100% down (0)	0.21	0.00	0.21	90%	0.48M	0.05	0.12	0.17	74%	0.58M	0.011	0.005	0.016	76%	6.3M
All the above															
All HIGH values	0.56	0.05	0.61	262%	0.16M	0.14	0.24	0.38	164%	0.26M	0.031	0.015	0.046	220%	2.2M
All LOW values	0.16	0.00	0.16	69%	0.63M	0.04	0.12	0.16	68%	0.63M	0.008	0.005	0.013	64%	7.6M
Changes to parameters liable to change over time:															
Prevalence															
H: x1.5	0.21	0.04	0.24	105%	0.41M	0.05	0.27	0.33	139%	0.31M	0.011	0.015	0.026	124%	3.9M
L: x0.5	0.21	0.01	0.22	95%	0.45M	0.05	0.09	0.14	61%	0.70M	0.011	0.005	0.016	76%	6.3M
Incidence in RDs															
H: x1.5	0.31	0.02	0.34	145%	0.30M	0.08	0.18	0.26	111%	0.39M	0.016	0.010	0.026	126%	3.8M
L: x0.5	0.10	0.02	0.13	55%	0.78M	0.03	0.18	0.21	89%	0.48M	0.005	0.010	0.015	74%	6.5M
New donor proportion															
H: x1.5 (16.5%)	0.23	0.03	0.26	113%	0.38M	0.06	0.23	0.29	125%	0.34M	0.011	0.012	0.024	115%	4.2M
L: x0.5 (5.5%)	0.18	0.01	0.20	85%	0.51M	0.04	0.13	0.17	71%	0.60M	0.010	0.007	0.017	83%	5.8M
Test sensitivity															
L: 1-sensitivity halved	*NA: sensitivity 100% in "best"*					0.05	0.12	0.17	74%	0.58M	0.011	0.007	0.018	88%	5.5M
LL: sensitivity 100%						0.05	0.06	0.11	48%	0.90M	0.011	0.005	0.016	76%	6.4M
Window period for test															
20% down	0.18	0.02	0.20	87%	0.50M	0.04	0.18	0.22	96%	0.45M	0.009	0.010	0.019	90%	5.4M
50% down	0.13	0.02	0.16	67%	0.64M	0.03	0.18	0.21	89%	0.48M	0.005	0.010	0.015	74%	6.5M
All the above															
All HIGH values	0.34	0.05	0.39	170%	0.25M	0.09	0.35	0.44	188%	0.23M	0.017	0.019	0.036	173%	2.8M
All LOW values	0.06	0.01	0.06	28%	1.5 M	0.01	0.02	0.03	13%	3.2 M	0.003	0.002	0.004	21%	23.4M
All parameters (except "new infections")															
All HIGH values	0.47	0.10	0.57	247%	0.17M	0.13	0.47	0.59	254%	0.17M	0.025	0.028	0.054	258%	1.9M
All LOW values	0.05	0.00	0.05	20%	2.2 M	0.01	0.00	0.01	3%	12.8 M	0.002	0.000	0.002	10%	50.0M
Variation				12-fold					76-fold					27-fold	

HBV

The estimates for risk of HBV infected donations entering the blood supply were most affected by changes in the rate of incidence of HBV, or any parameters that affected the estimated incidence rate. Reasonable variation in the "uncertain" parameters resulted in highest and lowest risk models with total estimates that were 3.8-fold different, from 1 in 625,000 donations to 1 in 125,000 donations. Reasonable variation in the "changeable" parameters resulted in highest and lowest risk models with total estimates that were 6.1-fold different, from 1 in 1.5 million to 1 in 254,000 donations. When reasonable variations in all the parameters used in the sensitivity analyses were combined (excluding variation in "new infections" so as to not duplicate the effect of error in the incidence rate), the highest and lowest risk models gave total estimates that were 12-fold different, from 1 in 2.2 million to 1 in 0.17 million donations. These are the very outside expected limits of the risk estimates.

HCV

The estimates for risk of HCV infected donations entering the blood supply were most effected by changes in the prevalence of anti-HCV, and in parameters such as test sensitivity that were combined in the model to estimate the number of anti-HCV positive donations released due to test or process error. Reasonable variation in the "uncertain" parameters resulted in highest and lowest risk models with total estimates that were 2.4-fold different, from 1 in 629,000 donations to 1 in 261,000 donations. Reasonable variation in the "changeable" parameters resulted in highest and lowest risk models with total estimates that were 14-fold different, from 1 in 3.2 million to 1 in 228,000 donations. When reasonable variations in all the parameters used in the sensitivity analyses were combined (excluding variation in "new infections" so as to not duplicate the effect of error in the incidence rate), the highest and lowest risk models gave total estimates that were 76-fold different, from 1 in 12.8 million to 1 in 0.17 million donations. These are the very outside expected limits of the estimates.

HIV

The estimates for risk of HIV infected donations entering the blood supply were most affected by changes in the rate of incidence of HIV, or any parameters that affected the estimated incidence rate. Reasonable variation in the "uncertain" parameters resulted in highest and lowest case models with total estimates that were 3.5-fold different, from 1 in 7.6 million donations to 1 in 2.2 million donations. Reasonable variation in the "changeable" parameters resulted in highest and lowest case models with total estimates that were 8.4-fold different, from 1 in 2.8 million to 1 in 23 million donations. When reasonable variations in all the parameters used in the sensitivity analyses were combined (excluding variation in "new infections" so as to not duplicate the effect of error in the incidence rate), the highest and lowest case models gave total estimates that were 27-fold different, from 1 in 50 million to 1 in 1.9 million donations. These are the very outside expected limits of the estimates.

5.4 Discussion

Sensitivity analyses

Reasonable variation in "uncertain" parameters affected the estimates by 2 to 4 fold. This is not a significant amount of variation. However, variation in the "changeable" parameters resulted in a much greater range of estimates – with up to more than 70-fold variations. The particularly wide range of estimates produced for HCV resulted from the sensitivity of the HCV model to the prevalence of infection. It is not unrealistic to include a 50% reduction in anti-HCV prevalence, as the prevalence of anti-HCV did fall by over 50% during the period studied. These results suggest that lowering the prevalence of HCV in blood donations, or improving the detection of anti-HCV positives (by improved test sensitivity, reduction of lab error rate) is the most fruitful avenue for reducing the total risk of donations from HCV infected donors entering the blood supply. One qualifying point about this risk is that not all of these donations – and more so for HCV than for HBV and HIV – will be infectious. Seventy-five percent of anti-HCV positive donors are HCV RNA positive by PCR, and it is probable that only RNA positive donations will transmit infection to recipients. The HCV risk estimates could therefore by reasonably reduced by multiplying the "error" component by 0.75. This would give a "best" overall estimate of 0.19

per 100,000 (1 in 533,000) and a highest risk of 0.48 per 100,000 (1 in 210,000). (As the lowest risk model sets sensitivity to 1 and error to 0, no error component exists).

In contrast, for HBV and HIV the incidence of infection and parameters that affect the risk of window period donations had the greatest effect on the risk estimates. This suggests that for these infections – with very low prevalence already achieved in the donor population - the most fruitful avenues to reduce the risk further are strategies to reduce the number of seroconversion in donors, and reductions in the window period of tests.

The use of the incidence method without adjustment for longer periods between donations for seroconverters can result in considerable overestimation of the risk of window period donations. This may partially explain observations of lower risk than predicted - for example after the introduction of p24 ag testing in the US.

The prevalence and incidence rates of blood-borne viruses in English blood donors during 1993-1995 were very low. Seroconversion rates for HIV and HCV were less than one tenth the rates reported for 1991-1993 at five USA blood centres (Schreiber , 1996), and less than one sixth the rates reported for 1992-1994 in France (Courouce, 1996). Low prevalence of these infections in the UK, and current donor education and selection appears to be effective in securing relatively small numbers of seroprevalent donors and, as far as we can identify, seroconverting donors to the English National Blood Service. Current tests for anti-HIV, anti-HCV and HBsAg have high sensitivity and are performed by automated processes with stringent quality and process control procedures and computerised information transfer. Overall, therefore, the risk of infectious donations entering the blood supply is extremely small. Testing sero-negative donations, or components, for viral nucleic acids may have the potential to provide a direct measurement of infectious donations entering the blood supply *(see below)*. Prospective assessment of recipients is one way to directly measure rates of viral transmission from blood components. However, as the low risks of infection transmission now make the required size of such studies to accurately estimate risk prohibitive, a theoretical approach has been taken to estimating the number of infectious donations that may enter the blood supply from English blood centres. There are several potential sources of error in the

data, and in the assumptions, used in this study. These errors may have led to over- or under-estimation of the true risk.

The estimates of risk associated with window period donations are highly dependent on accurate and complete identification of seroconversion in blood donors. The definition of a seroconversion in a repeat donor required detailed information about the first sero-positive donation and the last sero-negative donation. If this information was absent, a true seroconversion may have been excluded from this study. Our seroconversion rates, and therefore risks, may be underestimates. The sensitivity analysis showed that exclusion of "possible" seroconversions could - if all possible seroconversions were true seroconversions - have led to underestimation of the window period risk.

Blood components that are produced from repeat donor donations are associated with lower risks than similar components from new donors. The methods used to estimate the incidence of infections in new donors made various assumptions - for example, that the incidence rate of HIV and HCV was constant over different age groups, and that the ratio of incidence amongst new and repeat donors had been constant since 1986 for HIV and since 1992 for HCV. These assumptions are unlikely to be valid, and considerable uncertainty therefore surrounds the estimates of the risks of window period donations from new donors. The use of several different methods to generate an estimate of the new donor risk multiplier gives some security against the errors of any one method, but does not necessarily improve the accuracy of the resulting measure of increased risk. Although new donors contribute only 11% of all donations, they contribute a larger proportion to the total risk estimates. The sensitivity analysis showed that the use of different new donor incidence multipliers caused the window period risk estimates to vary by plus or minus approximately 15%.

The inter-donation interval between seroconversion is longer than the average inter-donation interval; the average inter-donation interval for the 13 HCV seroconversions detected during 1993-95 was 63 weeks. This will tend to lead to overestimation of window period risk by the incidence method unless an appropriate adjustment is made. The adjustment used produced the same window period risk estimates as an alternative method of estimating the window period risk. Studies that have used the incidence methods without similar adjustment, and have included seroconversion with inter-donation intervals that

differ from the rest of the donor population will have over, or under, estimated the risk. Even with this adjustment made, the estimates are still sensitive to the inter-donation interval.

The transient nature of HBsAg causes several complications to estimating the risk of window period donations from HBV infected donors. Other studies that have assumed that the observed inter-donation interval for donors who seroconvert for HBsAg is also characteristic of donors who acquire HBV infection but never donate during their HBsAg positive period of infection may have over estimated the risk of window period donations from donors with HBV infection.

Donors who donate during an infectious window period, but do not re-attend to give a post-seroconversion sero-positive donation may contribute infectious donations to the blood supply that would not have been included in these estimates. Indeed, there are plausible reasons why donors may be more likely to donate only, or for the last time, during an infectious window period. Despite alternative testing options and donor education, people who have a self-perceived exposure risk may attend donation sessions in order to obtain infection tests, and these donation attendances may occur in the sero-negative window period. Also, in the course of a donation attendance a donor may become aware that he/she is not eligible to donate due to a recent exposure risk. One English blood centre has a confidential donation exclusion option to allow donors to declare exposure risks in confidence and withdraw their donation from the blood supply without taking any non-routine action (Brennan, 1995). If this option is not utilised, and at sessions where it is not available, a donor with an exposure risk may find it easier to proceed with his/her current donation attendance and self-defer from further donation.

A process error rate of 0.5% was used. Donation testing and release is largely automated and computerised in English blood centres and the probability of an error may well be considerably lower than 0.5%. The error risk contributes 24%, 26% and 2% to the overall risk for HIV, HCV and HBV infectious donations respectively. Sensitivity of tests used during the study period was taken as 99% for HCV tests and 99.5% for anti-HIV tests. Test failure consequently accounted for 24% and 52% of the total HIV and HCV risks respectively.

Since the introduction of anti-HCV testing in 1992, the prevalence of anti-HCV in donations from repeat donors has declined steeply as seroprevalent donors have been removed from the donor panel. The majority of anti-HCV positive repeat donors detected during 1993-1995 were first-time tested donors. The prevalence of anti-HCV in donations from repeat donors is expected to continue to decline until all repeat donors have been tested for anti-HCV. The estimated risk due to sero-positive donations from repeat donors is therefore also expected to decrease. This was shown in the comparison between the first and second three-year period of study. While the risk of window period donations dependent on seroconversions remained constant, the risk of errors and test failures dependent on the prevalence of infection fell.

There is an additional theoretical risk of HIV and HCV infection, not included in our estimates, from sero-negative infectious donations from donors with no detectable antibody to these infections.

In contrast to HCV and HIV, the estimated risk for HBV infectious donations is relatively high when compared to published risks from the USA. This may be largely due to a difference in donation testing strategy. Testing for hepatitis B core antibody is routine in the USA, and some other European blood services. This additional test was introduced, before a specific test for HCV infection was available, as a surrogate marker for a risk of HCV infection. However, where implemented, it also served to remove the risk of HBV infectious donations entering the blood supply due to HBsAg sero-negative donations from donors with anti-HBc and evidence of HBV infectivity. The detection of tail-end carriers by HBsAg tests is expected to have improved in recent years as the sensitivity of HBsAg tests has increased; the ratio of observed tail end to acute transmitters that was used may therefore be out-of-date and resulting in overestimation of the risk of infectious, HBsAg negative donations from tail end carriers.

The additional safety that may be gained by strategic policy changes such as more stringent donor selection, donation testing or by performing viral inactivation procedures on tested components may be estimated by appropriate alteration to the data and assumptions used in the calculations described. The low level of the current risk estimates and the considerable uncertainty

surrounding them, implies that predicting the benefits of additional safety measures will be difficult to do with certainty, and that observing any future improvement in the viral safety of blood components from English blood centres will be even more difficult. Variations in estimates are easily obtained by changing methods and assumptions and the estimates are more sensitive to changes in some of these factors than to changes in observed prevalence and incidence rates.

Findings of different results from the different methods to estimate the new donor multiplier, and from different methods to estimate the window period risk using English data may not be experienced when these methods are applied to other data. In general, the methods used would be more robust in countries with higher prevalence and incidence. The estimates for England are relatively fragile and vulnerable to errors in assumptions and to errors in generalisations. It is now accepted that prospective studies cannot accurately measure the risk of transfusion-transmitted infection in the UK. It may also be the case that calculations described above also lack the precision to accurately detect the true risks in the UK - at least not with accuracy good enough to, for example, evaluate the relative expected benefit from two alternative approaches to improving blood safety.

Donations from new donors were associated with a higher risk of prevalent, and of incident, infection than donations from repeat donors. Donations from new donors constituted only 11% of tested blood donations during the study period, but made a significant contribution to the total risk. New donors accounted for 33%, 62% and 38% of the estimated number of donations entering the blood supply each year from donors with HIV, HCV and HBV infections. Studies that do not consider the risk from new donors are likely to underestimate the total risk.

Comparison with observed, reported transmissions

Several additional factors need to be considered in order to estimate the number of recipients infected as a result of these donations from infected donors. These factors include the infectivity of the donations, the number of components made from each donation, the percentage of untransfused components, the number of components to which each recipient is exposed, the

prevalence of immunity in recipients and the rate of infection from transfused components. Recognition of transfusion transmitted HIV, HCV and HBV is impaired because of the occurrence of sub-clinical infections, long lag periods between infection and disease onset and is also obscured by high mortality from other causes. Furthermore, transfusion may not be suspected as the cause of even clinically apparent post-transfusion infections, and suspected transfusion transmitted infections may not come to the attention of the blood transfusion service. Furthermore, donors are encouraged to notify the blood centre if they are ill in the weeks following donation. Reported symptoms of acute hepatitis or HIV seroconversion illness may therefore lead to withdrawal from the blood supply of infectious donations from seroconverting blood donors, and a consequent reduction in the risk to recipients. The effect of such prompted withdrawals of potentially infected components has not been quantified.

Since HIV antibody testing of blood donations began in the UK, one HIV infectious donation to the Scottish National Blood Service has been detected by the observation of seroconversion in a donor, with subsequent identification of infection in a recipient in the UK (Crawford, 1987) and one HIV infectious donation to the English National Blood Service has been detected by the observation of infection in a recipient and subsequent identification of a seroconversion in a donor (Martlew, 2000). Three cases of transfusion transmitted HCV infection by HCV antibody tested blood donations have been reported.

Table 5.11 shows the risk estimates alongside observed rates of clinically recognised cases and the results of a recent prospective study of the recipients or almost 22,000 blood components (Regan, 2000).

Table 5.11 Sources of quantitative data and estimates in the UK about how many transfusion-transmitted infections occur (or are reported)

Infection	Surveillance of apparent cases, 1995-1999 (see PTI surveillance - chapter 4 *)	Prospective study of transfusion recipients, approx. 22,000 donations (Regan, 2000) [95% CI]	Estimated infectious donations released into the blood supply per year, 1993-98 [ranges]
HAV	1 (Hewitt,1997)	NA	NA
HIV	1 (3 recipients infected)	0 [0 - 423]	0.5 [0.3 – 0.9]
HCV	2	0 [0 - 423]	6 [5 – 9]
HBV	5	0 [0 - 423]	24 [9 – 74]
HTLVI&II	0	0 [0 - 423]	NA
Bacteria	11	NA	NA

NA = Not available.

The estimates derived from calculations predict more transmission by transfusion than are clinically recognised. This discrepancy can be explained by poor ascertainment of cases for a number of reasons. It was estimated in 1987 by Mortimer et al, that 50% of blood components were transfused to patients who were dead within one year. High mortality in the post-transfusion period has been observed more recently in the cohort of patient traced in the course of the HCV Lookback programme (Robinson, 2001) in which - amongst those reported to have died - 47% died within one year of their transfusion. Patients who die shortly after their transfusion are unlikely to receive diagnoses of a transfusion-transmitted infection during this time. Severe disease - due to the underlying reason for transfusion, and, or, symptoms caused by treatments may obscure the clinical presentation of transfusion-transmitted infections and make their diagnosis - even if symptomatic - less likely. Many transfusion-transmitted infections are likely to be asymptomatic for many years. Some infections may occur in patients who have other more probable risk factors for infection and so transfusion is never investigated as the source.

Both of the HCV infections and one of the HBV infections that have been clinically recognised, and reported between October 1995 and September 1999 (see Chapter 4) were detected by the blood service identifying an infected

donor, not by diagnoses in the recipients, who until contacted and offered testing, were unaware of their infection.

The estimates suggested that 85% of donations entering the blood supply from donors with HBV, HCV or HIV infection were donations from donors with HBV. 63% (five of eight) of reported transfusion-transmitted HBV, HCV and HIV infections were HBV.

The estimates suggested that 6% of donations entering the blood supply from donors with HBV, HCV or HIV infection were due to process error: 1 of 8 (12.5%) reported transfusion-transmitted HBV, HCV and HIV infections were due to process error.

5.5 Post-script re recent developments in donation testing

Continuing concern about the safety of blood, and continuing advances in testing assays and technologies, has led to new, additional tests being proposed for all blood donations, and to one new assay – for HCV nucleic acid – being introduced in England and Wales. The methods of estimation described above have recently been used to predict the yield of nucleic acid testing for HCV and to evaluate the expected benefits of other new testing strategies. This post-script includes some of this work, and demonstrates the use of the risk estimation methods that have been described in this thesis to inform discussions about strategies for testing blood donations.

Combined HIV antibody and antigen tests

Combined tests for anti-HIV and HIV p24 antigen are now available and have been approved for use for donation testing in England. These tests have been shown to shorten the time from infection to test positivity by around 4 days. These tests will be expected to reduce the risk of window period donations from HIV infected donors by 27% (see sensitivity analysis above)

HCV NAT testing

Nucleic acid testing (NAT) of pools of 96 donation samples began in England in early 1999. The system used combines the Qiagen (Hilden, Germany) extraction system, using the Qiagen robotic processor (Bio Robot 9604, Qiagen), with the Roche Amplicor HCV version 2.0 assay using the automated COBAS system. Results of sensitivity testing using Roche Amplicor

2.0 assay, following the probit analysis approach recommended by the Paul Ehrlich Institute, identifies that when a pool of 96 donations is used, the 95% detection limit will be 2,000 IU/mL in the donation (Harrison, unpublished data). (NB. The relationship between Genome Equivalents (geq) and International Units (IUs) is approximately 1IU to 4 geq for the National Institute for Biological Standardisation and Control working standard.)

NAT of 2 million donations during 1999 yielded 1 anti-HCV negative, HCV NAT positive donation

NAT testing might be expected to detect a proportion of the risk estimated above due to the window period of early infection - by using NAT window rather than serology window i.e. only 20 rather than 59 days, 66% of HCV serology window period detected. NAT testing is also expected to detect the proportion of the false negative component of the risk estimates above that are viraemic as well as serologically positive. This can be estimated by multiplying the false negative risk estimate by the proportion of prevalent infections that are expected to be viraemic i.e. 75% for HCV, 100% for HIV. NAT would also detect any truly sero-negative, viraemic infections - assumed to be negligible in the estimates above.

The expected findings of NAT testing (plus truly sero-negative, viraemic infections) in England are shown in Table 5.12.

Table 5.12 Expectations for findings of HCV and HIV NAT.

Component of risk	Estimates 1996-98 **HIV** NATposWP 7d % viraemic: 100%	**HCV** NATposWP: 39d % viraemic: 75%
i. window period risk	0.0079: 1 in 13M *(26% of total)*	0.0229: 1 in 4.4M *(19% of total)*
ii. false negative risk		
test failure	0.0177: 1 in 5.6M	0.0671: 1 in 1.5M
process error	0.0043: 1 in 23M	0.0332: 1 in 3.0M
Total	0.0299: 1 in 3.3M	0.1232: 1 in 0.8M

The 90% confidence intervals on an observation of 1 in 2 million is 1 in 40 million to 1 in 0.4 million, i.e. the observed rate during 1999 was consistent (statistically, at the 10% significance level) with a true rate of 0.05 to 4.75 per 2 million. Table 5.13 shows the probabilities of observing 1 or fewer positives in a sample size of 2 million for different “true” rates.

Table 5.13 Poisson probabilities.

"True" rate	Sample tested	p of observing up to 1
1 per 0.5 million (i.e. 4 in 2 million)	2 million	p = 0.091
1.0 per million (i.e. 2 in 2 million)	2 million	p = 0.406
0.5 per million (i.e. 1 in 2 million)	2 million	p = 0.735

The estimates were therefore not significantly different from the observation during 1999. However, the observed rate would have had to be many times higher than expected for a difference to be apparent. Some possible reasons for estimates of HCV infectious donations being *overestimates* are shown in Table 5.14. The most likely reason for *underestimation* of risk by the method used was underestimation of HCV incidence in repeat donors based on seroconversions (i.e. if all seroconversions were not detected). Other possible reasons for underestimation of HCV risk include occurrence of anti-HCV negative, PCR positive donors during chronic infection, and the opposite of all the reasons shown in Table 5.14.

Table 5.14 Reasons why the assumptions/data used in estimates of the frequency of infectious donations entering blood supply in England could overestimate the observed frequency of NAT positive donations.

Reason	Evidence
• NAT negative "eclipse" period during anti-HCV negative window period, i.e. infectious window shorter.	• Some evidence of this from US studies.
• Test sensitivity better than 99% and error rates less than 0.5%.	• ? thought probable by test experts.
• Prevalence of anti-HCV in donations has fallen.	• Observed in UK - fall of 25% between 1993-95 and 1995-97.
• Seroconverting donors have a longer inter-donation interval (between sero-negative and sero-positive donation) than average donors do. The model may not fully adjust for this.	• Observed in UK data (1.4 times longer) and in EPFA survey data (personal communication Konstanze Muller-Breitkreutz).
• New donor risk multiplier overestimated.	• None available, however, evidence for estimated multiplier was weak.
• Some anti-HCV positive donations are not infectious i.e. are NAT negative.	• Only 75% of anti-HCV positive donors with PCR test results are PCR positive.
• Rate of seroconversion in donors has fallen.	• None.

NAT is expected to prevent (and measure) a proportion of estimated risk of donations from infected donors not detected by serology. This proportion is estimated as approximately 74% for HCV and 80% for HIV. The probability of the observed findings of HCV NAT (1 in 2 million), if estimates (revised, 1996-98) are correct, is 0.1 - 0.4. The observed findings suggest true risk may be lower than estimated - one possible reason for this - worth further investigation - is incorrect assumption about donation patterns following infections (this has been observed in other voluntary donor populations). Alternatively, the error and false negative component of the models could be too high.

In order to estimate the impact of a range of new tests/strategies on the release of infectious donations into the blood supply, these models were extended with some extra parameters regarding the performance of proposed additional tests, to estimate the infectious donations that could be prevented from entering the blood supply by the use of additional tests. The assumptions made (in addition to those described earlier in this chapter), and the results are given below.

For each yield the "best" estimates - generated from calculations using the "most likely" parameter values - and the results of "high" and "low" calculations (or models, or scenarios) giving the best and worst yields that can be expected, were calculated. For some parameters there was very little evidence for the correct values to use. This is partially reflected in the ranges of values used in the "high" and "low" models (or scenarios).

Different scales were needed on the graphs to express the risks and yields for each infection. To ease comparison of the yield estimates, all the yield graphs are plotted on the same scale in the final figure. This still leaves differences in the severity of the infections averted, and differences in the costs of the interventions for the reader - and for further work - to consider.

New models were constructed, using only the parameters shown below, for HTLV and bacteria. Ranges were also calculated using parameter values that applied for different donation (i.e. from new or repeat donors), or component (e.g. platelets, or red cells), types where applicable.

Although the aim of this work was the evaluation of testing strategies, donor selection is an important alternative strategy to reduce infectious risk, and

an indication of the effect it can have on the risks calculated was included as follows.

Infected donors who report (after donation and diagnosis of their infection) a history that should have led to exclusion from blood donations accounted for approximately 20% of all infected (HBsAg, anti-HCV or anti-HIV) donations collected during 1996-98. Table 5.15 below shows the potential reduction in prevalence and incidence of HBsAg, anti-HIV and anti-HCV that would be obtained if these donors were successfully excluded from donating blood.

Table 5.15 Reduction that could be achieved by excluding PRE-donation all donors who report (POST-donation) a history of sex between men or a history of injecting drug use, and all donors who have had a previous positive donation (based on infected donors reported in England and Wales, 1996-98).

	HBsAg	Anti-HCV	Anti-HIV
Reduction in prevalence	4%	27%	23%
Reduction in incidence	5%	7%	26%

This is an underestimate of the reduction in risk that could be achieved by better compliance with existing donor selection criteria because i) only the permanent exclusion criteria were considered, ii) there is likely to be some underreporting of these risk factors post-donation.

The risks of HBV, HCV and HIV infectious donations were re-calculated after reducing the prevalence and incidence data by these amounts – to show the minimum reduction in risk that could be achieved by improved donor selection. The point estimates of these risks ("Risk: with improved donor selection") are shown on the graphs.

Another alternative strategy – inactivation – has not been considered. This could be added to the models in the future, or considered as a potential strategy to prevent the remaining risk.

HIV

The following additional tests were considered: -

a) anti-HIV/HIV p24 antigen combined tests

b) HIV NAT for DNA on single samples

c) HIV NAT for RNA on pooled (48) samples

d) HIV NAT for RNA on single samples

The extra assumptions used (those with * are varied below) in the "best" model were: -

II. All false anti-HIV negative donations and antibody positive donations released in error are negative for HIV antigen, positive for HIV PCR (both RNA and DNA, in single and pooled samples).

III. * Combined anti-HIV/HIV Ag assays will detect new infections 4 days before current anti-HIV tests (3rd gen ELISAs) (i.e. giving total WP of 18 days, infectious WP of 11 days).

IV. * HIV NAT for DNA on single samples will detect new infections 6 days before.

V. current anti-HIV tests (i.e. giving total WP of 16 days, infectious WP of 9 days).

VI. * HIV NAT for RNA on pooled samples will detect new infections 10 days before current anti-HIV tests (i.e. giving total WP of 12 days, infectious WP of 5 days).

VII. * HIV NAT for RNA on single samples will detect new infections 12 days before current anti-HIV tests (i.e. giving total WP of 10 days, infectious WP of 3 days).

The "high" model estimated the highest yield consistent with the probable limits of the assumptions used, and the "low" model estimated the lowest yield consistent with the probable limits of the assumptions used. The assumptions used and varied are shown below.

Assumption	***High model***	***Best model***	***Low model***
Anti-HIV/HIV Ag benefit	5 days	4 days	3 days
HIV DNA single benefit	7 days	6 days	5 days
HIV RNA pooled benefit	12 days	10 days	8 days
HIV RNA single benefit	14 days	12 days	10 days
Prevalence anti-HIV	10% increase	Observed 1996-98	10% decrease
Incidence HIV	10% increase	Observed 1996-98	10% decrease
	High model #2		***Low model #2***
Donations tested	New donors	All/average	Repeat donors

HCV

The following additional tests were considered:-

a) HCV Ag tests (in addition to anti-HCV)

b) HCV NAT for RNA on pooled (48) samples

c) HCV NAT for RNA on single samples

The extra assumptions used (those with * are varied below) in the "best" model were: -

II. All false anti-HCV negative donations and antibody positive donations released in error are negative for HCV antigen, and 75% are positive for HCV PCR (both single and pooled samples).

III. * HCV Ag assays will detect new infections 53 days before current anti-HCV tests (3rd gen ELISAs) (i.e. giving total WP of 13 days, infectious WP of 6 days).

IV. * HCV NAT for RNA on pooled samples (48) will detect new infections 55 days before current anti-HCV tests (i.e. giving total WP of 11 days, infectious WP of 4 days).

V. * HCV NAT for RNA on single samples will detect new infections 57 days before current anti-HCV tests (i.e. giving total WP of 9 days, infectious WP of 2 days).

The "high" model estimated the highest yield consistent with the probable limits of the assumptions used, and the "low" model estimated the lowest yield consistent with the probable limits of the assumptions used. The assumptions varied are shown below.

Assumption	***High model***	***Best model***	***Low model***
HCV Ag benefit	58 days	53 days	48 days
HCV RNA pooled benefit	56 days	55 days	54 days
HCV RNA single benefit	58 days	57 days	56 days
Prevalence anti-HCV	10% increase	Observed 1996-98	10% decrease
Incidence HCV	10% increase	Observed 1996-98	10% decrease
	High model #2		***Low model #2***
Donations tested	New donors	All/average	Repeat donors

HBV

The following additional tests were considered:-

a) anti-HBV core tests

b) HBV NAT pooled (48) samples

c) HBV NAT on single samples

The extra assumptions used (those with * are varied below) in the "best" model were:

II. * All donations collected during the HBsAg negative, infectious, window of late acute infection are anti-HBV core positive.

III. All donations collected during the HBsAg negative, infectious, period at the tail-end of HBV carriage are anti-HBV core positive.

IV. All HBsAg positive donations released in error are anti-HBV core positive and are HBV NAT positive (both single and pooled samples).

V. * HBV NAT on pooled samples (48) will detect new infections 6 days before current HBsAg tests (i.e. giving total WP of 53 days, infectious WP of 47 days).

VI. * HBV NAT on single samples will detect new infections 15 days before current HBsAg tests (i.e. giving total WP of 44 days, infectious WP of 37 days).

VII. * The risk of infectious donations from tail-end carriers is in ratio to the risk from acute infections as observed amongst reported transfusion-transmitted HBV cases in England and Wales during 1991-97 when 11 of 14 cases were due to tail-end carriers. The detection of tail-end carriers by HBsAg tests is expected to have improved in recent years as the sensitivity of HBsAg tests has increased, this ratio may therefore be out of date – making the "low" model closer to today's reality.

The "high" model estimated the highest yield consistent with the probable limits of the assumptions used, and the "low" model estimated the lowest yield consistent with the probable limits of the assumptions used. The assumptions varied are shown below.

Assumption	*High model*	*Best model*	*Low model*
Late acute window period	50 days	30 days	10 days
HBV NAT pooled benefit	9 days	6 days	3 days
HBV NAT single benefit	18 days	15 days	12 days
Prevalence HBsAg	10% increase	Observed 1996-98	10% decrease
Incidence HBV	10% increase	Observed 1996-98	10% decrease
Tail-end:acute ratio	15:3	11:3	3:3
	High model #2		***Low model #2***
Donations tested	New donors	All/average	Repeat donors

Bacteria

A new model was constructed to estimate the number of contaminated donations expected to be detected/prevented by the following strategies if applied in England and Wales:

a) revised donor arm cleansing

b) diversion of first mls

c) testing of platelets

The assumptions used (those with * are varied below) in the "best" model were:

II. * 1 in 1700 red cell units and 1 in 200 platelet units are contaminated with bacteria

III. * Revised donor arm cleansing would prevent 50% of contaminations of all units.

IV. * Diversion would prevent 50% of contaminations of all units.

V. * Testing all platelets pre-release would prevent 80% of contaminated platelets.

The "high" model estimated the highest yield consistent with the probable limits of the assumptions used, and the "low" model estimated the lowest yield consistent with the probable limits of the assumptions used. The assumptions varied are shown below.

Assumption	*High model*	*Best model*	*Low model*
Contamination frequency in red cell units	10% increase	1 in 1,700	10% decrease
Contamination frequency in platelets	10% increase	1 in 200	10% decrease
Prevented by arm cleansing	65%	50%	35%
Prevented by cleansing and diversion	65%	50%	35%
Detection by testing	99%	80%	50%
	High model #2		***Low model #2***
Units	Platelets	All	Red cells

Please note: Not all contaminations are of equal importance/severity, but all are treated as equal in the model above. This model could be refined to consider endogenous bacteria and skin contaminants separately. As endogenous bacteria are more often associated with serious complications in recipients, and are not prevented by arm cleansing or diversion, this may clarify comparison of the yield of platelet testing vs cleansing and diversion.

HTLV

A new model was constructed to estimate the yield of the following strategies for testing for HTLV infection if applied in England and Wales:

a) anti-HTLV testing pooled samples

b) anti-HTLV testing single samples

The assumptions used (those with * are varied below) in the "best" model were:

-

II. * The prevalence of HLTV infection in blood donations is 2 per 50,000 donations.

III. * Leucodepletion reduces the prevalence of infectious donations by two-thirds.

IV. * The sensitivity of anti-HTLV tests is 98% in single samples, 92% in pooled samples (48).

The key assumptions and ranges are shown in the table.

Assumption	*High model*	*Best model*	*Low model*
HTLV prevalence in donors	1 in 20,000 (LSE)	1 in 50,000	1 in 100,000 (Scotland)
Reduction by leucodepletion	50%	67%	95%
Sensitivity of anti-HTLV tests I. single samples II. pooled samples	99.5% 95%	98% 92%	95% 88%
Reduction in infectivity due to leucodepletion	50%	66%	95%

This simple model could be expanded to consider the incidence of HTLV infection in blood donors and then used to additionally estimate the yield of proposed applications of the test such as:-

I. Anti-HTLV testing all donors once only

II. Anti-HTLV testing all donors once, and then repeating testing at specified time intervals

RESULTS

The results are shown in the tables below – expressed first as number of donations tested to prevent one infectious donation, and then as the number of infections prevented per million donations tested.

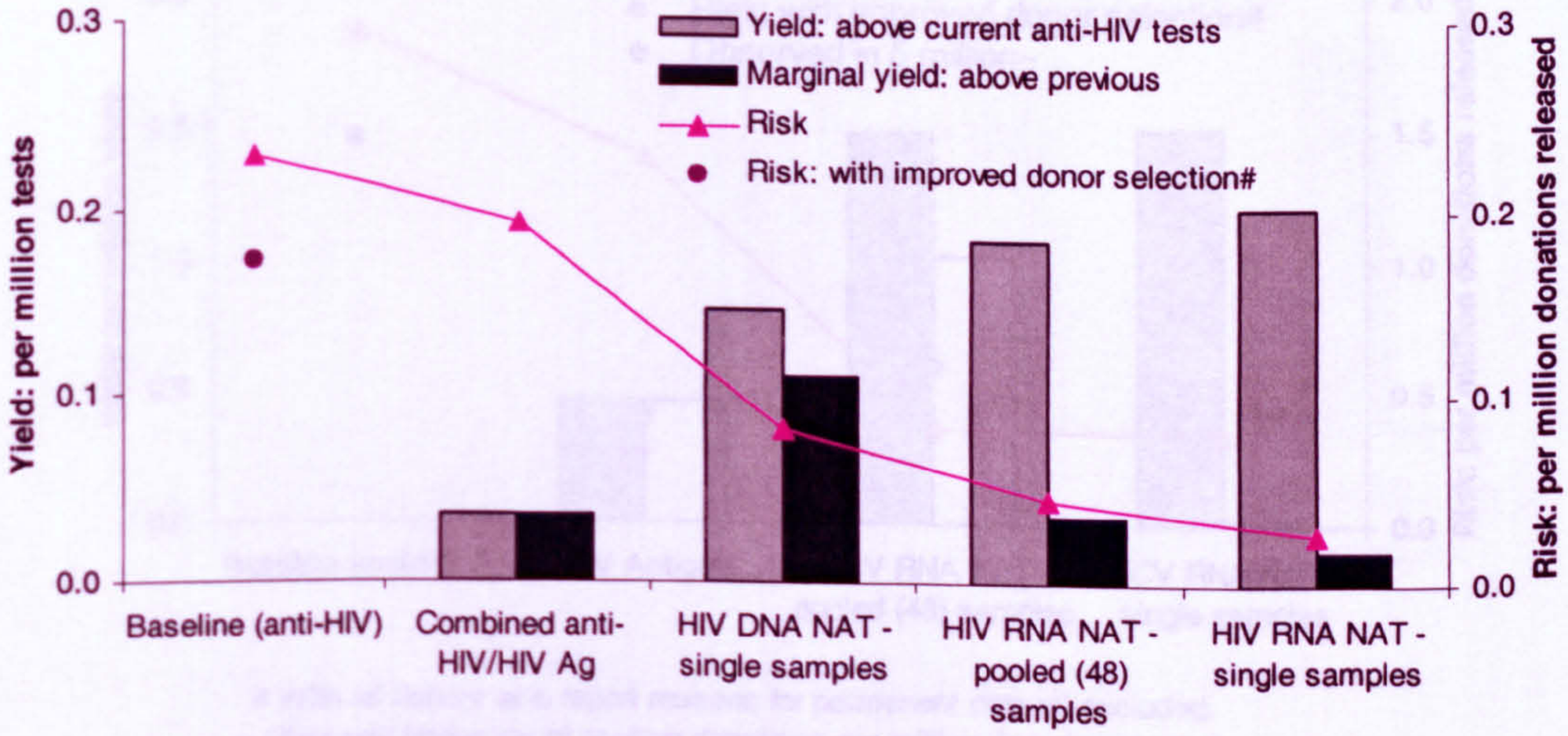
Table 5.16 Donations tested (millions) to prevent 1 HIV infectious donation.

Additional test added	*Yield: above current anti-HIV tests*	*Marginal yield: above previous*	*Leaving a risk of 1 in x million*
Combined anti-HIV/HIV Ag	27.5	27.5	5.2
Range: high & low yield assumptions	20.0 To 40.8	20.0 To 40.8	5.0 To 5.5
Range#2: new & repeat donors (best model assumptions)	13.8 To 31.6	13.8 To 31.6	1.4 To 7.9
HIV DNA NAT - single samples	6.8	9.0	12.2
Range: high & low yield assumptions	5.8 To 8.0	8.2 To 10.0	12.5 To 12.2
Range#2: new & repeat donors (best model assumptions)	1.6 To 11.5	1.8 To 18.0	6.1 To 14.0
HIV RNA NAT - pooled (48) samples	5.4	27.5	22.0
Range: high & low yield assumptions	4.5 To 6.7	20.0 To 40.8	33.4 To 17.5
Range#2: new & repeat donors (best model assumptions)	1.5 To 8.4	13.8 To 31.6	11.0 To 25.2
HIV RNA NAT - single samples	5.0	55.0	36.7
Range: high & low yield assumptions	4.1 To 6.1	50.0 To 61.1	100.1 To 24.5
Range#2: new & repeat donors (best model assumptions)	1.4 To 7.4	27.6 To 63.1	18.4 To 42.1

Table 5.17 HIV infectious donations prevented per million donations tested.

Additional test added	*Yield: above current anti-HIV tests*	*Marginal yield: above previous*	*Leaving a risk of x per million*
Combined anti-HIV/HIV Ag	0.04	0.04	0.19
Range: high & low yield assumptions	0.05 to 0.02	0.05 To 0.02	0.20 to 0.18
Range#2: new & repeat donors (best model assumptions)	0.07 to 0.03	0.07 To 0.03	0.71 to 0.13
HIV DNA NAT - single samples	0.15	0.11	0.08
Range: high & low yield assumptions	0.17 to 0.12	0.12 To 0.10	0.08 to 0.08
Range#2: new & repeat donors (best model assumptions)	0.62 to 0.09	0.54 To 0.06	0.16 to 0.07
HIV RNA NAT - pooled (48) samples	0.18	0.04	0.05
Range: high & low yield assumptions	0.22 to 0.15	0.05 To 0.02	0.03 to 0.06
Range#2: new & repeat donors (best model assumptions)	0.69 to 0.12	0.07 To 0.03	0.09 to 0.04
HIV RNA NAT - single samples	0.20	0.02	0.03
Range: high & low yield assumptions	0.24 to 0.17	0.02 To 0.02	0.01 to 0.04
Range#2: new & repeat donors (best model assumptions)	0.72 to 0.13	0.04 To 0.02	0.05 To 0.02

Figure 5.3 HIV – estimated yield (best model) infectious donations per million.



With all donors who report reasons for permenent deferral excluded.

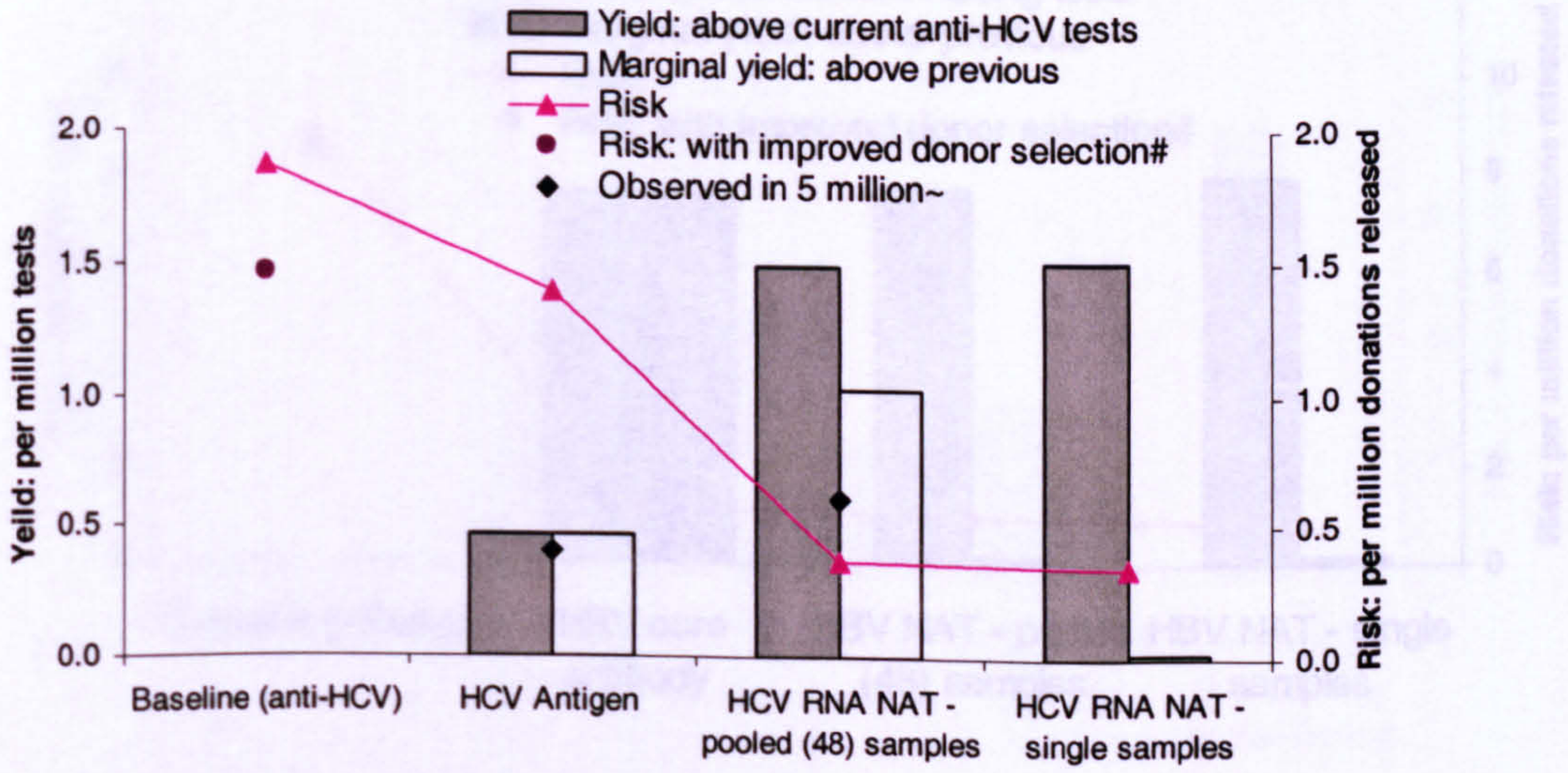
Table 5.18 Donations tested (millions) to prevent 1 HCV infectious donation.

Additional test added	*Yield: above current anti-HCV tests*	*Marginal yield: above previous*	*Leaving a risk of 1 in x million*
HCV Antigen	2.15	2.15	0.72
Range: high & low yield assumptions	1.79 to 2.64	1.79 to 2.64	0.67 to 0.77
Range#2: new & repeat donors (best model assumptions)	0.56 to 3.41	0.56 to 3.41	0.12 to 2.18
HCV RNA NAT - pooled (48) samples	0.67 [1]	0.97	2.71
Range: high & low yield assumptions	0.61 to 0.75	0.92 to 1.05	2.52 to 2.94
Range#2: new & repeat donors (best model assumptions)	0.12 to 1.61	0.16 to 3.03	0.45 to 7.83
HCV RNA NAT - single samples	0.66	57.04	2.85
Range: high & low yield assumptions	0.60 to 0.74	51.86 to 63.38	2.65 to 3.08
Range#2: new & repeat donors (best model assumptions)	0.12 to 1.58	14.71 to 90.48	0.46 to 8.57

Table 5.19 HCV infectious donations prevented per million donations tested.

Additional test added	*Yield: above current anti-HCV tests*	*Marginal yield: above previous*	*Leaving a risk of x per million*
HCV Antigen	0.46	0.46	1.39
Range: high & low yield assumptions	0.56 to 0.38	0.56 to 0.38	1.49 to 1.29
Range#2: new & repeat donors (best model assumptions)	1.80 to 0.29	1.80 to 0.29	8.69 to 0.46
HCV RNA NAT - pooled (48) samples	1.49	1.03	0.37
Range: high & low yield assumptions	1.65 to 1.33	1.09 to 0.95	0.40 to 0.34
Range#2: new & repeat donors (best model assumptions)	8.24 to 0.62	6.44 to 0.33	2.25 to 0.13
HCV RNA NAT - single samples	1.51	0.02	0.35
Range: high & low yield assumptions	1.67 to 1.35	0.02 to 0.02	0.38 to 0.32
Range#2: new & repeat donors (best model assumptions)	8.31 to 0.63	0.07 to 0.01	2.18 to 0.12

Figure 5.4 HCV – estimated yield (best model) infectious donations per million.



With all donors who report reasons for permenent deferral excluded.
~ Observed frequency of positive donations per million donations tested.

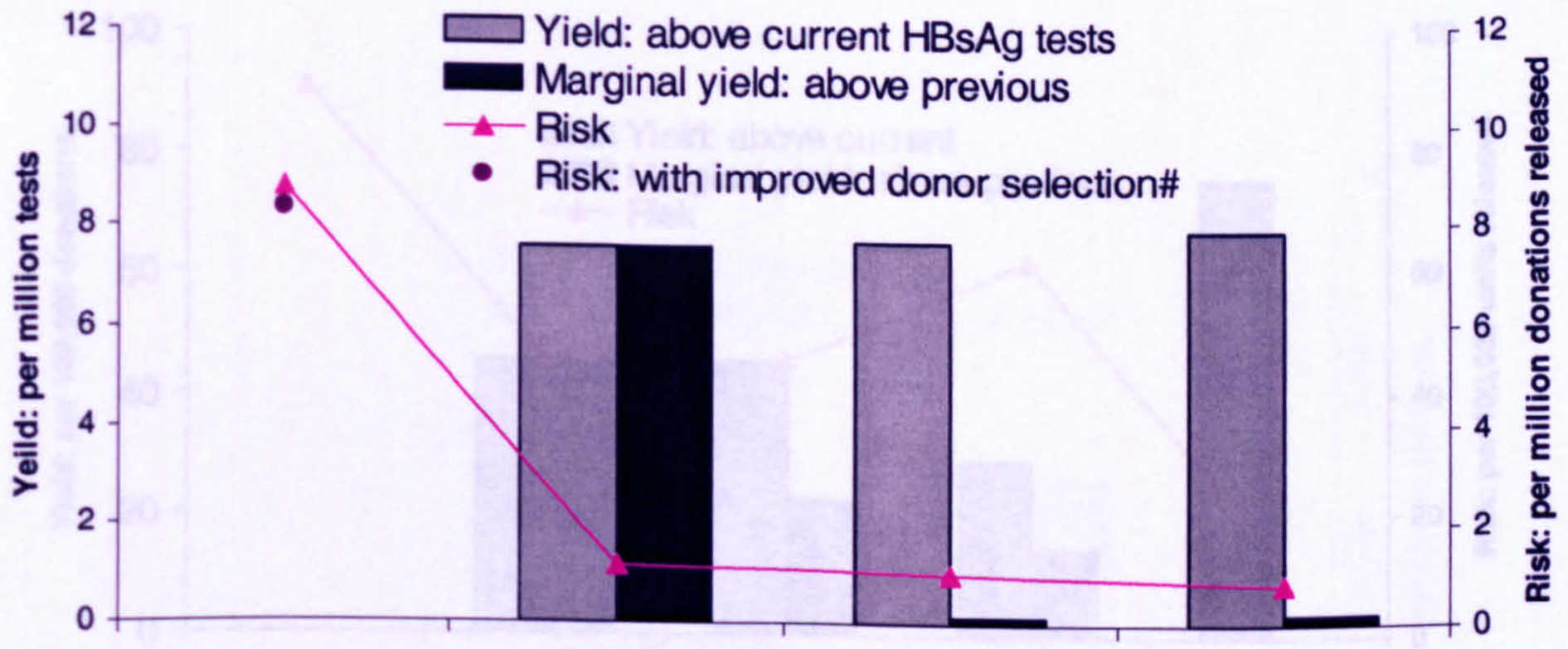
Table 5.20 Donations tested (millions) to prevent 1 HBV infectious donation.

Additional test added	*Yield: above current HBsAg tests*	*Marginal yield: above previous*	*Leaving a risk of 1 in x million*
HBV core antibody	0.13	0.13	0.85
Range: high & low yield assumptions	0.06 to 0.34	0.06 to 0.34	0.77 to 0.95
Range#2: new & repeat donors (best model assumptions)	0.04 to 0.18	0.04 to 0.18	0.30 to 1.11
HBV NAT - pooled (48) samples	0.13	7.37	0.96
Range: high & low yield assumptions	0.06 to 0.34	4.47 to 16.38	0.94 to 1.00
Range#2: new & repeat donors (best model assumptions)	0.04 to 0.17	2.64 to 9.58	0.34 to 1.25
HBV NAT - single samples	0.13	4.92	1.20
Range: high & low yield assumptions	0.06 to 0.33	4.47 to 24.58	1.18 to 1.05
Range#2: new & repeat donors (best model assumptions)	0.04 to 0.17	1.76 to 6.39	0.43 to 1.55

Table 5.21 HBV infectious donations prevented per million donations tested.

Additional test added	*Yield: above current HBsAg tests*	*Marginal yield: above previous*	*Leaving a risk of x per million*
HBV core antibody	7.56	7.56	1.18
Range: high & low yield assumptions	16.29 to 2.91	16.29 to 2.91	1.29 to 1.06
Range#2: new & repeat donors (best model assumptions)	22.24 to 5.67	22.24 to 5.67	3.28 to 0.90
HBV NAT - pooled (48) samples	7.70	0.14	1.04
Range: high & low yield assumptions	16.52 to 2.98	0.22 to 0.06	1.07 to 1.00
Range#2: new & repeat donors (best model assumptions)	22.62 to 5.78	0.38 to 0.10	2.90 to 0.80
HBV NAT - single samples	7.90	0.20	0.84
Range: high & low yield assumptions	16.74 to 3.02	0.22 to 0.04	0.85 to 0.96
Range#2: new & repeat donors (best model assumptions)	23.19 to 5.93	0.57 to 0.16	2.34 to 0.64

Figure 5.5 HBV – estimated yield (best model) infectious donations per million.



With all donors who report reasons for permenent deferral excluded.

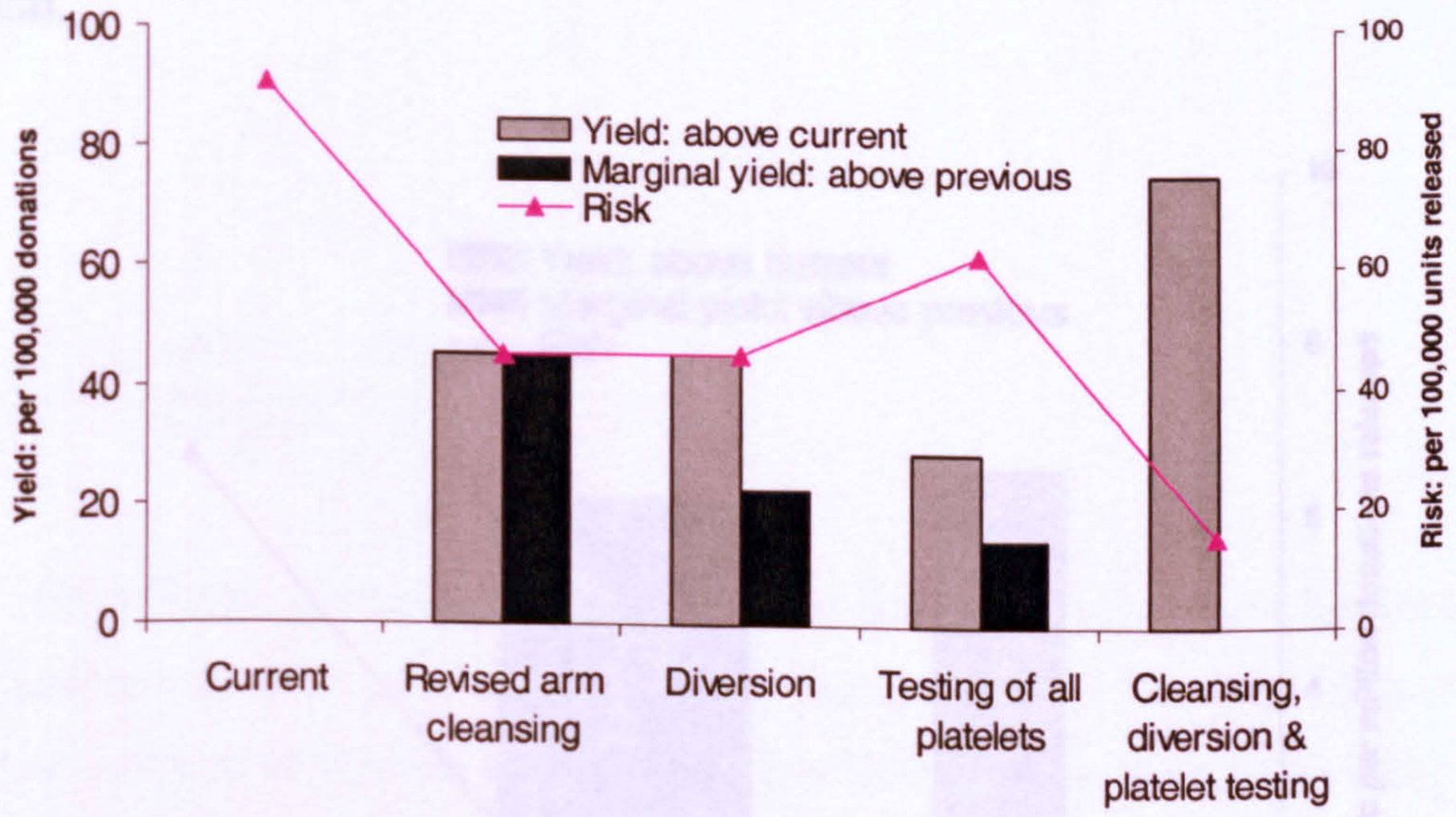
Table 5.22 Donations tested (100,000s) to prevent 1 bacterially contaminated unit.

Additional test added	*Yield: above current*	*Marginal yield: above previous*	*Leaving a risk of 1 in x 100,000s*
Revised arm cleansing	0.022	0.022	0.022
Range: high & low yield assumptions	0.015 to 0.035	0.015 to 0.035	0.029 to 0.019
Range#2: platelets & RBCs (best model)	0.004 to 0.034	0.004 to 0.034	0.004 to 0.034
Diversion	0.022	0.044	0.022
Range: high & low yield assumptions	0.015 to 0.035	0.082 to 0.029	0.029 to 0.019
Range#2: platelets & RBCs (best model)	0.004 to 0.034	0.008 to 0.068	0.004 to 0.034
Testing of all platelets	0.035	0.069	0.016
Range: high & low yield assumptions	0.031 to 0.038	0.090 to 0.059	0.015 to 0.018
Range#2: platelets & RBCs (best model)	0.003 to 0.000	0.005 to 0.000	0.010 to 0.017
Cleansing, diversion & platelet testing	0.013	-	0.065
Range: high & low yield assumptions	0.012 to 0.018	- -	0.059 to 0.036
Range#2: platelets & RBCs (best model)	0.002 to 0.023	- -	0.040 to 0.068

Table 5.23 Bacterially contaminated units prevented per million donations.

Additional test added	*Yield: above current*	*Marginal yield: above previous*	*Leaving a risk of x per 100,000*
Revised arm cleansing	45	45	45
Range: high & low yield assumptions	65 to 29	65 to 29	35 to 53
Range#2: platelets & RBCs (best model)	250 to 29	250 to 29	250 to 29
Diversion	45	23	45
Range: high & low yield assumptions	65 to 29	12 to 35	35 to 53
Range#2: platelets & RBCs (best model)	to	to	to
Testing of all platelets	29	14	62
Range: high & low yield assumptions	32 to 26	11 to 17	68 to 56
Range#2: platelets & RBCs (best model)	400 to 0	200 to 0	100 to 59
Cleansing, diversion & platelet testing	75	-	15
Range: high & low yield assumptions	83 to 54	- to -	17 to 28
Range#2: platelets & RBCs (best model)	475 to 44	- to -	25 to 15

Figure 5.6 Bacteria – estimated yield (best model) contaminated units per 100,000.



NB. The yeild shown here does not distinguish between contaminations from donors' venepuncture, and contaminations due to endogenous bacteria. Only platelet testing prevents the release of units contaminated with endogenous bacteria, or during processing.

Table 5.24 Donations tested (millions) to prevent 1 HTLV infectious donation.

Additional test added	*Yield: above current*	*Marginal yield: above previous*	*Leaving a risk of 1 in x million*
Anti-HTLV test donations in pools (48)	0.16	0.16	1.88
Range: high & low yield assumptions	0.18 to 0.15	0.18 to 0.15	0.80 to 16.67
Anti-HTLV test each donation	0.15	2.50	7.50
Range: high & low yield assumptions	0.15 to 0.15	0.89 to 28.57	0.80 to 16.67

Table 5.25 HTLV infectious donations prevented per million donations tested.

Additional test added	*Yield: above current*	*Marginal yield: above previous*	*Leaving a risk of x per million*
Anti-HTLV test donations in pools (48)	6.13	6.13	0.53
Range: high & low yield assumptions	5.42 to 6.61	5.42 to 6.61	1.25 to 0.06
Anti-HTLV test each donation	6.53	0.40	0.13
Range: high & low yield assumptions	6.54 to 6.64	1.13 to 0.04	1.25 to 0.06

Note: Preliminary work in Scotland suggests that the loss of sensitivity resulting from pooling can be reduced, without incurring specificity problems, by adjustment of the cut-off (to below manufactuerers criteria). If so, the yield for pools would approach that calculated for single samples.

Figure 5.7 HTLV – estimated yield (best model) infectious donations per million.

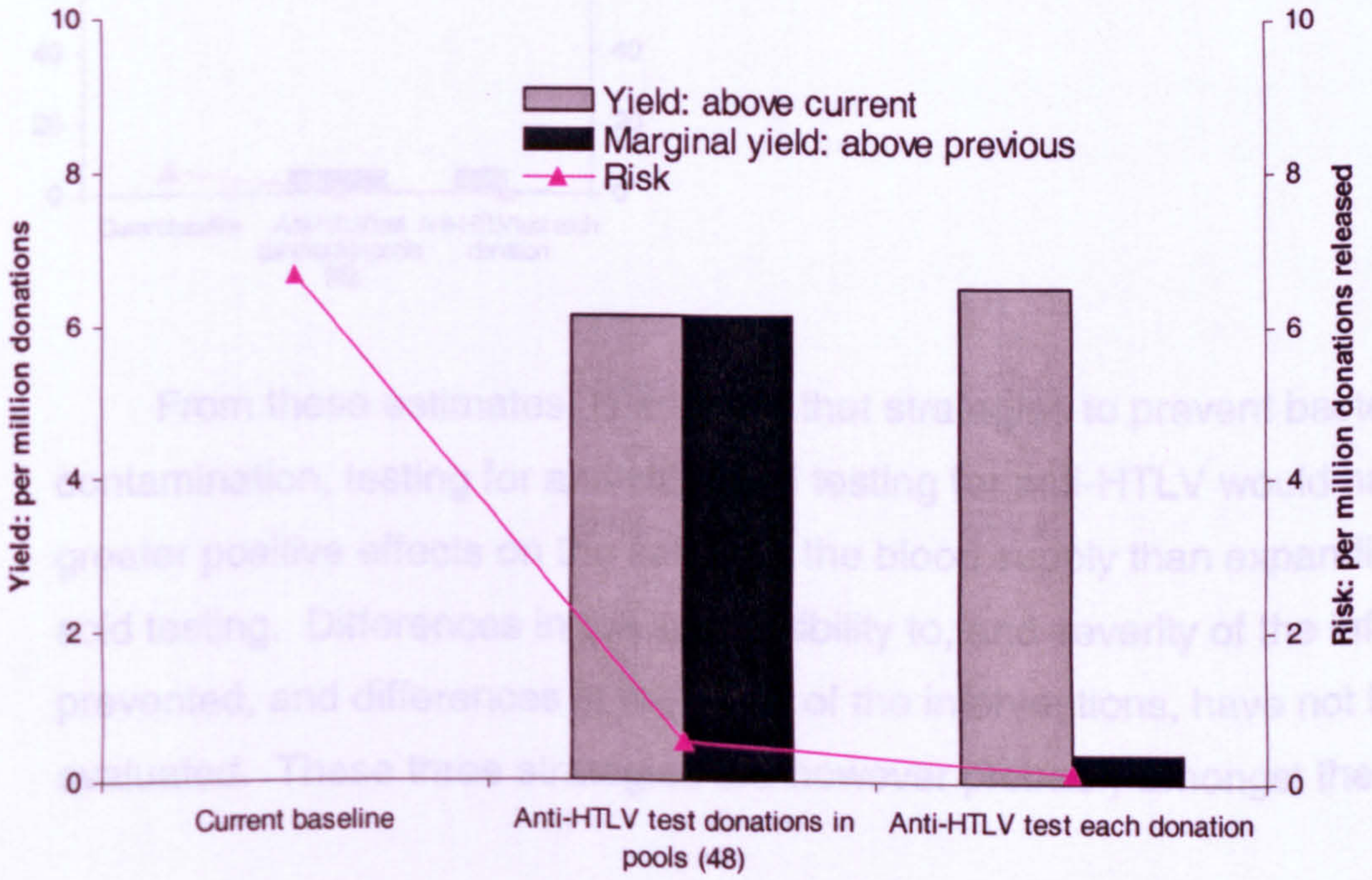
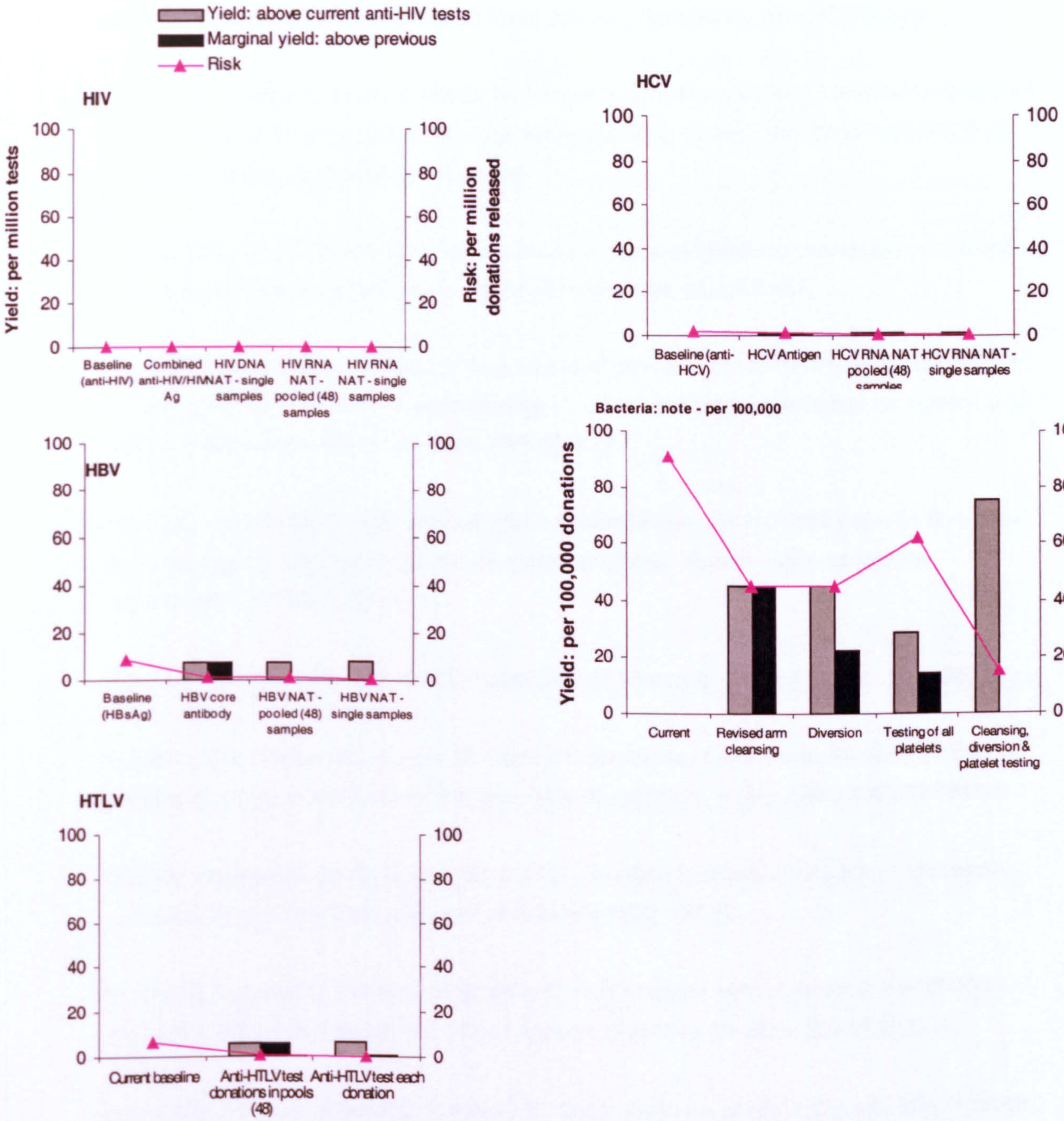


Figure 5.8 Re-production of graphs with same scale (except Bacteria)



From these estimates, is appears that strategies to prevent bacterial contamination, testing for anti-HBV and testing for anti-HTLV would have greater positive effects on the safety of the blood supply than expanding nucleic acid testing. Differences in the susceptibility to, and severity of the infections prevented, and differences in the costs of the interventions, have not been evaluated. These three strategies are however probably amongst the cheapest

considered. Bacteria have caused more reported transfusion-associated deaths in recipients than all other infectious risks in recent years (chapter 4).

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Chapter 6. Discussion & Conclusion

Discussion

By way of summary and conclusion, I will review the TTI surveillance and related studies described in this thesis and discuss further work that could contribute to blood safety and public health knowledge.

Adequacy and limitations of the surveillance system established

The work described has established ongoing and systematic collection, analysis and interpretation of data relevant to blood safety and the epidemiology of HBV, HCV and HIV in blood donors. Timely data from this system are disseminated regularly to a wide range of colleagues and organisations responsible for the control and prevention of these infections. This work therefore meets the criteria for surveillance (e.g. Last JM, 1988).

Some aspects of this surveillance system are atypical. In particular, the aims of the post-transfusion infection surveillance require a high degree of completeness and accuracy in the data collected for each reported case, and do not include the detection of changes in trend or distribution. In these respects it is more akin to a collation of case histories than a classical surveillance system. The time lag between the occurrence of an incident and the availability of complete information reported to the post-transfusion infection surveillance system mean that this surveillance is not expected to prompt timely control measures for any individual case. The contribution to control measures is via provision of information for more general priority setting and the evaluation of practices. These features are characteristic of enhanced surveillance systems of rare conditions, where fewer, more accurate, data are needed. Also, the ongoing, standardised, nature of the data collection and the regular dissemination of data can be used to justify its description as surveillance.

The two most obvious limitations of the post-transfusion infection surveillance are the unknown extent of under-reporting, and the poor likelihood of detecting transfusion-transmitted infections that cause either delayed-onset conditions or conditions that are not yet associated with blood-borne infectious agents. The former is a common problem for infectious disease surveillance. As discussed in chapter 1, prospective studies to inform this are not currently feasible in England and Wales except to estimate a maximum transmission rate, and therefore a maximum underreporting rate. The most recent study found no HBV, HCV or HIV transmissions amongst 22,000 donations, giving an upper estimate of transmission of 1 in about 500 units transfused. Observed transfusion-transmitted infections are very rare. The discrepancy between expected infectious donations released and observed infections although large, is not more than can be explained by a combination of under-diagnosis and under-reporting. How this partitions between under-diagnoses and under-reporting is not known. One source of information about underreporting of post-transfusion infections has been the HCV lookback. In the course of tracing and testing recipients, several HCV infected recipients were identified who had had post-transfusion hepatitis that had never been reported to the blood service. This pre-dated the surveillance system described and may or may not be similar today. Increased awareness of post-transfusion infections due to both the HCV/lookback experience and to the publicity of the SHOT system mean, hopefully, this is less likely to still occur. The risk estimations described in this thesis are another avenue to estimate under-diagnosis and under-reporting.

Much of the published literature about the estimation of the remaining risk of HBV, HCV and HIV from transfusion does not consider three aspects of the risk of infectious donations entering the blood supply that this thesis show to be important. Firstly is the omission to consider donations from new donors. In England and Wales, and elsewhere, there is evidence that new donors have a higher risk of both prevalent and incident infections. Although new donors only contribute 12% of donations in England and Wales, their donations contribute between one-third and two-thirds of the risk of HBV, HCV or HIV infectious donations entering the blood supply. Secondly, many studies have not considered the risk of false negative donations entering the

blood supply due to test sensitivity less than 100% or due to errors. The risk of window period donations is likely to dominate in situations of relatively low prevalence and high incidence. However, in situations as described in England and Wales, a significant proportion of the risk may be due to false negative test results. Thirdly, the most commonly used method does not adjust the risk estimation if seroconverting donors tend to leave a longer, or shorter, interval between donations than non-seroconverting donors. Again, the data analyses in this thesis show that this will result in overestimation, or underestimation of the risk respectively.

Rapid data from Donation Testing Surveillance does not benefit from detailed data of confirmatory test results and standardised classification of test results that follows. This has meant that the infection status of some donations has been incorrectly classified in the rapidly disseminated donation testing data. While this is not likely to have caused any significant errors in the summary data that are monitored, it has meant some inconsistencies – all be them minor - between early and subsequent data. It is planned that this will be avoided in future by obtaining confirmatory test results directly, and more rapidly, from a single laboratory that conducts all the confirmatory testing.

The exposure history information reported to the Infected Donor surveillance may be incorrect, or biased, for several reasons. Firstly, the information is usually self-reported by the infected donors. These donors may forget to mention exposures that are relevant, even when asked, or may choose to with-hold relevant information if they prefer either the member of staff they talk to, or the blood service to not know. In particular, this might be expected if the donor has an exposure history that was specified by the blood service as a reason to not donate blood. For example, 7% of HIV infected donors (1995-1999) who were reported by the blood service as having no identified risk factor, or with heterosexual sex as their probable route of infection where found by further investigations conducted by CDSC to have probably acquired their infections from sex between men. Secondly, each member of staff who records this information on the infected donor report form may have tendencies towards identifying, or recording, some risk factors more than others.

The monitoring of transfusion itself (who, why, how often etc) – could be seen as a component of the surveillance of blood safety. This is not routinely done in the UK but the data such monitoring would provide is increasingly sought after and would inform the blood service about changes in transfusion practices and requirements for components.

Opportunities for associated work

During the period of study described, several related areas of work have developed in collaboration with, if not directly dependent on, the surveillance system. In 1997, a register of individuals with a known date of HCV infection was established to study the natural history of HCV (Harris HE, 2000). This register initially consisted of HCV infected patients identified to be recipients of blood from donors subsequently found to be HCV infected, and presumed HCV infectious at the time of their donation to the infected recipient. Donors who seroconvert for anti-HCV between donations (within 3 years) are now also invited to enter this register to extend its observations to "known" date infections acquired by other routes.

Tissue donations collected by the English NBS centres have been increasing in both importance and numbers. In 1999, four centres started participating in a pilot system for the surveillance of infections in tissue donors that was established to run in parallel, and collect comparable data, to the blood donor surveillance. This is due to be expanded and extended in 2001.

Blood centre microbiology departments are equipped and skilled for the efficient running of tests on large numbers of samples. Several centres in the English NBS have taken on the testing of antenatal samples. Surveillance of antenatal HBsAg and anti-HIV testing is being established. These data are of use to public health work concerned with the control of sexually and vertically transmitted infections. They can also be used to inform the blood service of the prevalence of infections in the populations from which donors are drawn, and hence inform donor selection, and the success of donor selection in obtaining donations with a lowered prevalence of infection when compared to antenatal women.

Further work

The surveillance of Donation Testing will be improved by direct capture of data from the confirmatory laboratory and by feedback from the detailed reports for infected donors into a version of the donation testing database. This would allow the exclusion of certain groups of positive donations that do not actually represent an infection (e.g. donations from donors with HBsAg positivity due to recent immunisation, positive donations later shown to be due to contamination of the sample) from the testing data and so be more correct for true infection rates. The DT database would remain the most accurate for test specificity data, and the timeliest for infection rate data.

The surveillance of Infected Donors will be improved by follow-up of possible seroconverters and possible acute HBV or syphilis infections to enable routine, accurate, identification of donors with recent infections.
A programme of risk factor research with tested methods for follow-up of risk factors in donors with no identified risk, and evaluation of the risk associated with possible exposures reported by cases, would be a worthwhile extension of the information available from the surveillance. A case-control study protocol has been developed to investigate risk factors for HCV and HBsAg infection in donors with no identified risks reported. One hundred cases and two controls for each case would be needed to be expected to detect, with 5% significance and 80% power, relative risks for HCV infection of around 3-4, and relative risks for HBV infection of around 2-3, for exposures common to between 10% and 70% of controls. The methods of this study are currently being piloted on cases of seroconversion for anti-HCV or HBsAg with no identified risk reported. These cases are perhaps the most informative as they provide information about current risk factors, and information about the risk factors for donors who are most likely to donate during the window period of early infection.

Possible methods for investigating risk factors for positivity to tests for pre-symptomatic vCJD are being considered, with the aim being to design a study to investigate risk factors for positivity to tests for vCJD and conduct appropriate preparatory work so that such a study can go ahead without delay once a test becomes available. No test is currently available for vCJD, and in

the absence of a test, and of precisely identified risk factors within the UK population, there is no way to differentiate individuals who are more likely to be incubating infection from those less likely to be incubating infection. As soon as a test is available that identifies infection, or is even a rough surrogate for infection, this will change. The blood service is likely to use any available tests to try to exclude possibly infectious donations from the blood supply. There will be urgent interest in the use of the test to identify individuals, and numbers of individuals, in the population that may be at risk of disease/infectivity. There will also be urgent interest in the use of the test to investigate risk factors for infection (or possible infection) by comparison of test-positives with test-negatives. Unlike most blood-borne infections that have been major problems for blood transfusion, vCJD is unlikely to be associated with the same "high risk" groups that are now asked to not give blood. Blood donors have been an important population for initial investigation of risk factors for other infections e.g. HCV, but the selective nature of donors has meant these studies have been biased away from the more common risk factors in the population and have therefore been limited in their ability to inform public health. Blood donors are expected to be more representative of the general population with regard to their diet than with regard to their exposures to other blood borne infections. This makes the donor population a more suitable population for the investigation of risk factors for vCJD present in the general population than has been the case for other infections, for example, HCV and HIV. Also, in contrast to HCV and HIV, risk factors for vCJD seem to be less easy to identify by the epidemiology of the clinically diagnosed cases than has been true for HIV and HCV (to be expected if the risk factor is a relatively common dietary factor, and/or long past). It may therefore be the case that a test becomes available before good risk factor information is available for donor selection - and the test will be the tool (via epidemiological studies) for obtaining this information. The blood service may therefore be able to contribute to public health, and to blood safety through donor selection, by conducting a prompt study of risk factors associated with positivity to the first (and subsequent) tests for vCJD. Work on the design and methods of such possible studies could be done now,

to allow preliminary peer-review and preparation in advance of the time they are needed.

In order to improve the availability of safer blood, and prepare for any sudden drop in eligible donors (e.g. in case of poor specificity vCJD testing) and a need to recruit more donors and, or, relax some selection criteria in order to meet demands for blood, donor recruitment policy and donor selection criteria need to be evaluated. This requires combining knowledge about the response to recruitment drives and about the frequency of donor characteristics in potential donors, with knowledge of the risk (i.e. the prevalence and incidence) of blood-borne infections in sections of the population that are targeted for recruitment and in potential donors with characteristics leading to exclusion. This work is beginning. Factors used by the NBS to monitor the success of recruitment (and so determine recruitment policy) are being added to the variables used to describe infection rates so that recruitment can consider infection rates as well as donation yields when targeting advertising and incentives to donate.

PTI surveillance describes instances of recognised TTI and identifies the circumstances under which they occur. Whilst the SHOT system has the potential to observe any novel symptom or syndrome occurring post-transfusion, its power to detect late-onset, chronic, or atypical symptoms of infections transmitted by transfusion is likely to be weak. For example, a rare malignancy associated with a viral agent not yet recognised to be an etiological factor for the malignancy. Studies of recipient mortality, and if possible morbidity, - ideally linked to stored samples from donations - could be used not only to test hypothesis about disease caused by transfusion transmissible agents, but also be used to data-dredge for any indication of unrecognised hazards of transfusion, and then for any infectious cause.

Blood components that are not transfused because they are visibly contaminated with bacteria should be returned to the blood service for investigation of the source, and any further spread, of the contamination. These events are not eligible for reporting to the PTI surveillance as there is

no transfusion and so no post-transfusion infection. However, these events can be just as informative about the source of contamination of blood components as a case of transmission and should be monitored. Surveillance of contaminated components (not transfused) could be seen as comparable – with regard to informing blood safety - to the surveillance of infections in donors, or the exercise performed by the SHOT system that has monitored "near-miss" events such as the transfusion of the "wrong" blood group that does not happen to cause a reaction.

Reconciliation of data in the TTI system and other CDSC information sources could be strengthened. For example, health care associated infections, and hospital-acquired bacteraemias are often reported as suspected transfusion associated infections. Different investigations concerning the same infection can currently be monitored by different departments of CDSC without awareness and exchange of information. Matching of records from different sources (e.g. laboratory reports, and infected donor reports) may become more difficult if personal identifiers collected by surveillance systems are further restricted. The ability to match reports should be retained so that information can be completed and updated from different sources and duplicate reports for a single infection can be identified.

The risk estimation methods are now being used to contribute to the evaluation of some transfusion service practices. Initial work on the evaluation of proposed new tests has been described (chapter 5). Further work will include the use of these methods in the evaluation of donor selection criteria. For example, the effect of accepting men who have had sex with men as blood donors on the risk of HIV and HBV entering the blood supply can be estimated using data and assumptions about the prevalence and incidence of HIV and HBV in this currently excluded group.

Overview of elements of a comprehensive (ideal) TTI surveillance system/programme for England and Wales and conclusion

The surveillance system for transfusion-transmissible infections in England and Wales is now relatively comprehensive. However, limitations and omissions can be identified when working with the data provided, or comparing the system with that in other countries.

The following components are proposed for a full and comprehensive TTI surveillance system for England and Wales. This is based on the system now in place. Other strategies could be combined to construct equivalent, alternative, total systems. For example, in France, where the current strategy is to actively follow-up every transfusion recipient, the benefits of a long-term recipient study would be far less and other supplementary strategies may be envisaged.

	Components of comprehensive TTI surveillance and epidemiology	***In England & Wales***
1.	Surveillance of infections in the population – including vigilance for mutant/variants of known infectious agents and for new infectious agents.	Currently conducted by PHLS & CDSC
2.	Surveillance of behaviours associated with infections in the population	Currently conducted by CDSC/ONS/special surveys e.g. the sexual lifestyles survey
3.	Surveillance of donation testing, infected donors and of (diagnosed, reported) post-transfusion infections.	Currently conducted by NBS/PHLS CDSC – as described in this thesis.
4.	Surveillance of non-infectious complications of transfusion	Currently conducted by SHOT.
5.	Infected recipient natural history studies.	Currently conducted for HCV infected recipients by PHLS CDSC.
6.	Infected donor risk factor investigations/studies	Routine investigations conducted by PHLS CDSC for HIV infected donors. Pilot study underway for HBsAg and anti-HCV seroconverting donors.
7.	Regular studies or routine monitoring of the frequency of characteristics proposed as donor selection criteria amongst potential and actual donors.	No routine. Several ad hoc surveys have been conducted by the NBS.
8.	Regular studies or routine monitoring of recipient characteristics and transfusion practices and outcomes.	No routine. Development of one study now in progress in NBS.
9.	Regular studies or routine monitoring of the morbidity and mortality of transfusion recipients.	No routine. Development of one study of mortality now in progress in NBS.
10.	An archive of donation samples and linked recipient samples for the testing of hypothesis regarding the prevalence of new/emerging infections in blood donations and their transmission by transfusion. Ideally, this would be linked to 8 and 9 so that hypotheses about morbidity and mortality could also be tested.	No routine.

The surveillance of transfusion-transmissible infections forms a relatively small component of the surveillance of blood-borne infections, just as blood donation testing forms a relatively small component of the control of the

transmission of these infections in the population. Targeted HBV immunisation, needle-exchange schemes and safer sex practices do far more to reduce the transmission of HIV, HBV and HCV by addressing the more common routes of transmission of these viruses. Data from the surveillance of blood donors in England and Wales has not identified new high priorities for national public health work: it has informed public health about the frequency of infections in low risk, healthy adults (and in transfusion recipients) and thereby clarified the elevation of risks experienced by some other groups in the population and perhaps indirectly contributed to the setting of priorities for infection prevention.

The documentation of, and publicly available information about, transfusion-transmitted infections may actually adversely affect the perception of blood safety amongst at least some of the public. The identification and description of risks can lead to public worry, without the expected reassurance from the quantification of the risk. Further work is needed on risk communication and understanding how risks are perceived.

Infectious risks are no longer the major cause of preventable, serious, complications, however this remains a key area. This may be partly because the potential for damage to recipients is there, as has been revealed by HIV and HCV in the past two decades, and this danger – of known infections and of new and, or, unknown ones - is perhaps better perceived and more dreaded than the known risks of non-infectious complications. Several attempts have been, and continue to be, made to examine transfusion risks in a broader context and to improve communication of the risks of transfusion to the general public.

Chapter 6 references

Harris HE, Ramsay ME, Heptonstall J, Soldan K, Eldridge KP. The HCV National Register: towards informing the natural history of hepatitis C infection in the UK. *Journal of Viral Hepatitis* 2000; **7**: 420-427.

Last JM. A Dictionary of Epidemiology. 1988 OUP.

Appendices

Never give blood just to get an HIV test

If you do, you risk infecting other people. You can get a confidential HIV test from clinics for sexually transmitted diseases.

Who can I talk to?

If you are worried about HIV or hepatitis, there are several people you can talk to, such as the nurse or doctor at the transfusion centre or your GP. Or you could call the Helpline specially set up for advice and assistance on HIV and AIDS.

National AIDS Helpline: Freephone
0800 567123
(24 hour service)

Please open and read carefully before you donate.

United Kingdom Blood Transfusion Services

Produced by Department of Health
G78/036 3666 1P 3m Dec 95 (12)
CHLORINE FREE PAPER

NBTS 1406

DO NOT GIVE BLOOD

Without Reading This Leaflet

United Kingdom Blood Transfusion Services

Keep Blood Transfusion Safe

Thank you for volunteering to be a blood donor; your gift could save someone's life.

Blood transfusions are safer now than they've ever been because we take such care with donor screening. All donations are tested thoroughly for dangerous viruses, but some viruses like HIV and hepatitis B and C cannot always be detected at the earliest stages of infection.

In fact, very occasionally, it may take up to a year between the time someone is infected and the time it shows up in tests. This means your blood might not show any signs of infection but could still pass on a disease.

The chances of this happening are very small, but if there is any risk you could have been infected – please don't give blood.

This leaflet will help you decide if you have been at risk. If, after reading it, you are still unsure or you need help, please talk in complete confidence to the nurse or doctor at the session.

Or, if you need time to think about it, it's quite alright to make an excuse and leave the session without giving blood, and with no questions asked.

Remember – you can't get hepatitis, HIV or any other infection by giving blood.

You should NEVER give blood if:

you, or your partner are HIV positive

you carry the hepatitis B or C virus

you are a man who has had sex with another man, even 'safe sex' using a condom

you have ever worked as a prostitute

you have ever injected yourself with drugs, even once

You should not give blood FOR A YEAR after sex with:

a man who has had sex with another man (if you are female)

a prostitute

anyone who has injected themselves with drugs

anyone with haemophilia or a related blood clotting disorder who has received clotting factor concentrates

anyone, of any race, who has been sexually active in Africa* in the past year. This is because the main route of HIV infection there is heterosexual sex.

** apart from Morocco, Algeria, Tunisia, Libya or Egypt.*

Please do not give blood if you think you need a test for HIV or hepatitis, or if you have had sex in the past year with someone you think may be HIV or hepatitis positive.

If you have any doubts or questions, talk to the nurse or doctor.

NBS 2757624

NATIONAL BLOOD SERVICE

Surname: Group:

Forenames:

Title: D.O.B. Sex: Donor No:

Address:

Tel No:
Occupation:
Tel No. (day):

Outcome of Attendance
01 BLED (>50ml)
02 LOW Hb
03 OTHER SAMPLES ONLY
04 NOT BLED - NO NUMBERS
05 NOT BLED - NUMBERS ISSUED
06 NOT BLED - PACK LABELLED (<50ml)

Donation No.

CODE

TOTAL

AWARD

Attendance Outcome

Date

Panel

Sub Panel

Message for session slip:

P:
T:

MALARIA RISK INFORMATION

Area Visited ..... Date of return ../../..

Visitor ☐ Resident ☐

Malaria ☐ Febrile illness ☐ Date of recovery ../../..

APHERESIS - TYPE OF DONATION

Platelets only ☐ Plasma for fractionation ☐

Platelets & Plasma ☐ Therapeutic ☐

Plasma for FFP ☐ Other ☐

OTHER SESSION COMMENTS

Withdraw / Suspend until ../../..
(Delete as appropriate)

For the Attention of Centre Medical Staff ☐

Additional Letter Attached ☐

SET MEDICAL BAR ☐

PACK HOLD CODE

.....

Signature .....

PACK WEIGHT STATUS

Normal ☐
Underweight ☐
Overweight ☐

I have completed my duties in accordance with S.O.Ps	SIGNATURES
APHERESIS - Machine set-up by	
REGISTRATION	
HEALTH CHECK	
Hb SCREEN PASS ☐ LOW ☐	
SESSION Hb RESULTS	
VENEPUNCTURIST Local anaesthetic YES ☐ NO ☐	
BEDSIDE CARE	
FINAL PACK/SAMPLE CHECK	

Stick Unused

Donation Number Labels Here

FRM/NBS/DS/017/05(A)

DECLARATION BY DONORS

1 I have today read and understood the Blood Safety Leaflet. To the best of my knowledge I am not at risk of infection or of transmitting these infections.

2 I agree that my blood donation can be tested for HIV and other infections. I understand that if my donation gives a positive result for any of these tests I will be informed and asked to attend for further confirmatory tests & advice.

3 I understand the nature of the donation process and the possible risks involved, as explained in the Information Leaflet.

4 I entrust my donation to the UK Blood Services to be used for the benefit of patients.

Donor's Signature .....

Medical Notes: .....

.....

Accept ☐ Suspend until: ...../...../..... Withdraw ☐

Session Slip Text: .....

.....

.....

MO's Signature: ..... Date: ...../...../.....

CONSENT TO CONTACT GENERAL PRACTITIONER

I hereby give consent for my doctor to provide the UK Blood Service with any clinical information necessary to establish my eligibility to donate my blood or plasma to the UK Blood Services.

Donor Signature: ..... Date: ...../...../.....

GP's Name: .....

GP's Address: .....

.....

.....

FOR STAFF USE ONLY

PLEASE PRINT YOUR FULL NAME ..... AND ANSWER THE FOLLOWING QUESTIONS

FIRST TIME DONORS AND DONORS WHO HAVE NOT GIVEN FOR 2 YEARS		YES	NO	STAFF USE
1	Have you ever had a serious illness including hepatitis or jaundice?			
2	Have you ever had an operation?			
3	Before 1985 did you have any injections of human pituitary extracts such as growth hormones?			
4	Before August 1992 did you have any brain surgery or an operation for a tumour or cyst on the spine?			
ALL DONORS TO COMPLETE QUESTIONS 5-27				
5	Are you fit and well?			
6	Are you currently seeing or waiting to see a doctor/dentist/nurse or other health care professional?			
7	Are you taking any regular medication?			
8	Have you taken any other medication, including over the counter remedies such as aspirin, **in the last 5 days?**			
9	Have you been told that you should **never** give blood?			
10	Have you **ever** injected yourself with anything, including body building drugs?			
11	In the last 2 years have you had jaundice or hepatitis?			
12	Has anyone in your family had CJD (Creutzfeldt-Jakob Disease)			
13	Have you ever had malaria?			
14	Were you born or did you live in another country before you were 5 years old?			
15	Have you been to places other than Western Europe, Australia, New Zealand or North America in the last 12 months?			
16	Have you ever had any unexplained fever while abroad, or shortly after your return to the UK?			
17	Have you ever lived in or visited Central/South America?			
18	Have you ever felt unwell after giving blood?			

IN THE LAST YEAR, OR SINCE YOUR LAST DONATION		YES	NO	STAFF USE
19	Have you received blood yourself?			
20	Have you had acupuncture, ear, nose, body piercing, a tattoo or semi-permanent makeup?			
21	Have you had any injury which could have put you at risk of hepatitis or HIV?			
22	Have you had an operation or serious illness?			
IN THE LAST 4 WEEKS:				
23	Have you, to the best of your knowledge, been in contact with any infectious disease?			
24	Have you had any vaccinations or immunisations?			

You should never give blood if:

- you or your partner are HIV positive
- you carry the hepatitis B or C virus
- you are a man who has had sex with another man, even "safe sex" using a condom
- you have ever worked as a prostitute
- you have ever injected yourself, even once, with drugs (including body building drugs)
- you think you need an HIV or hepatitis test

25	**IS IT POSSIBLE THAT ANY OF THE ABOVE MIGHT APPLY TO YOU?**	YES	NO

You should not give blood for a year after sex with:

- a man who has had sex with another man (if you are a woman)
- a prostitute
- anyone who has injected themselves with drugs
- anyone with haemophilia or related blood clotting disorder, who has received clotting factor concentrates
- anyone of any race who has been sexually active in Africa in the past year (apart from Morocco, Algeria, Tunisia, Libya, Egypt)
- someone you think might be HIV or hepatitis positive

26	**IS IT POSSIBLE THAT ANY OF THE ABOVE MIGHT APPLY TO YOU?**	YES	NO

27	**DO YOU WISH TO SPEAK IN CONFIDENCE TO A DOCTOR OR NURSE**	YES	NO

NBS 2757624

If you become unwell within 2 weeks of your donation, please ring the donor helpline on 0345 711711 as soon as possible.

FRM/NBS/DS/017/04(B)

Month ____ Year ____

NATIONAL BLOOD SERVICE

INFECTION SURVEILLANCE

DONATION TESTING SURVEILLANCE

This folder is for recording and reporting of testing performed on blood and plasma donations taken during a calendar month.

Section 1 is for recording the number of donations tested during the calendar month.

Section 2 is for recording the number of initially reactive (by manufacturers criteria) donations for HBV, HCV, HIV and *T. pallidum* screening tests during the calendar month.

Section 3 is for recording the details of each donation tested (with donation date within the calendar month) and found to be repeatedly reactive to the screen (by manufacturers criteria), and, in addition, all other donations (except those specified below) sent for further testing in order to confirm an infection with HBV, HCV, HIV or *T.pallidum*. Please classify donors according to the donor type classification explained on the inside cover of this folder. Separate sheets for each marker of infection are included :

a) HBsAg (yellow)
b) anti-HCV (green)
c) anti-HIV (pink)
d) *T. pallidum* (old gold)

If a sample is sent to the confirmatory laboratory, please also record the confirmatory conclusion when it is received. Please record the test kit and batch number used for the repeat testing on each sheet and use separate sheets for each batch of test used for repeat testing of donations collected within the month. Please add additional sheets to this folder as needed.

Please **do not routinely include**[1] the following samples which may be sent from your laboratory for confirmatory testing:

i) samples taken to re-confirm an infection in a donor ie.'diagnostic' samples[2]
ii) donation samples referred for antibody quantitation for immunoglobulin preparation
iii) non-BTS samples eg. ante-natal samples, organ/tissue bank samples[2]
iv) donation samples referred due only to criteria for a special study
v) autologous donations[2]

[1] If you wish to include these samples on Section 3 sheets for your own records please do so and distinguish the entry by writing "CONF" or "SPECIAL" by the donation number column.
[2] These samples should also be excluded from Section 1 and Section 2.

During the second week following the end of the calendar month please send the top (blue) copies of Section 1, Section 2 and Section 3 a) yellow, b) green, c) pink & d) old gold to:

The Medical Director (Infection Surveillance),
National Blood Authority, Oak House, Reeds Crescent,
Watford, Herts. WD24 4QN

Use the second (same colour) copies of Section 3 sheets to record results of confirmatory tests. Please return these second copies along with the next month's top copies, even if some confirmatory results are still outstanding.

Please pass an Infected Donor Surveillance folder to the relevant medical officer for each donor with a newly confirmed infection.

The back (white) copy of each report should be kept in this folder as a local record.

continued overleaf

NOTES ON COMPLETING THE FORMS:

Donor type classification

Please apply the following criteria for classifying donations into donor type on Section 3 forms.

NEW	Donations from donors who have <u>never been tested</u> by a BTC for this blood borne infection. ie. from donors who have never before donated to a UK BTC, and from donors who have not donated since the introduction of testing for the marker to which they are now found to be reactive. Please note that this latter type of NEW donor in Section 3 would be classified as an OLD donor in Section 1. For these rare cases, please circle NEW *and* insert "ONT" (ie. old not tested) in the donor type box of Section 3.
Previously reactive (PR)	Donations from donors who are currently flagged donors/donors withdrawn from the panel due to at least one repeatedly reactive donation within the last six months, or at the last, or last-but-one donation. In practice this may include donors previously reactive to the current test and donors previously reactive to another test for the same marker used to test previous donations.
Not previously reactive (NPR)	Donations from donors who have been tested by the screening test before, but have either never been repeatedly reactive to the test, or who have not been repeatedly reactive at the last, or last-but-one donation or during the last six months ie. are not, at this time, flagged/withdrawn due to reactivity to the test.

Confirmatory laboratory conclusion

Please use the following meanings for the confirmatory laboratories' conclusions on Section 3 forms.

POS	Confirmed to be positive.
NEG	Confirmed to be negative.
UNDET	Confirmatory tests do not conclude that this donation is either positive or negative. The marker/infection status of the donation is concluded as UNDETERMINED.
ND	The confirmatory laboratory did not perform any confirmatory tests on this donation (for example, if it was decided that testing of a donation would not contribute any information towards concluding a donor's infection status according to the algorithm in use, or if the sample was spoilt on arrival at the confirmatory laboratory).

If you have any questions about the completion of these reports please call the CDSC/NBA Infection Surveillance Officer (Kate Soldan) on 020 8200 6868 x4602

: DONATION TESTING SURVEILLANCE

SECTION 1: Donation totals

BTC : [ ] Month [ ] Year [ ]

Please complete the table below as fully as possible. The totals for new and old/repeat donors (bold outlined boxes) are the minimum requirement. ***If*** age and sex breakdowns are also available please complete the entire table.

Number of donations tested :-

NEW DONORS	<25 years	25-34 years	35-44 years	45+ years	TOTAL
Males					
Females					
Total new					

OLD/REPEAT DONORS	<25 years	25-34 years	35-44 years	45+ years	TOTAL
Males					
Females					
Total old/repeat					

TOTAL DONATIONS TESTED					

Please try to exclude the four categories of donors listed below from the counts of donations from NEW donors, and please indicate whether these categories may have been *included* in NEW above by ticking 'Yes' or 'No'.

May NEW include : (Please tick)

i) new donors who attend a session, but **do not** provide a specimen for microbiological testing? . . . . . Yes ( )No ( )
ii) donors who have donated to other transfusion centres in the UK? . . . . . Yes ( )No ( )
ii) repeat donors who attend a session uncalled/without their donor certificate? Yes ( )No ( )
iii) lapsed donors ie. donors who have not donated for a certain number of years or more (eg. 2 or 5), please specify lapse period = ...years? . . . . . Yes ( )No ( )

Report completed by (please print name): _____ Date ____/____/____

Please return the top(blue) copy of this form along with Section 2 and Section 3 of this month's donation testing report to:- The Medical Director, (Infection Surveillance) National Blood Authority, Oak House, Reeds Crescent, Watford, Herts. WD1 1QH. Thank you for your help.

[Form code: DTS 1.01]

Month ____ Year ____

: DONATION TESTING SURVEILLANCE

SECTION 2: Donations initially reactive to screening tests

BTC : ____ Month ____ Year ____

Please complete the table below with the numbers of blood and plasma donations tested and the numbers found to be initially reactive (IR) (by manufacturers criteria) in screening tests for anti-HIV, HBsAg, anti-HCV and *T.pallidum* antibodies performed on donations obtained during this month. Please complete one line for each batch of kit used.

Marker screen & test (ie. write manufacturer/test kit name and generation)	Batch numbers of kits used	Initially reactive donations / Total donations tested
Anti-HIV Test kit:	_____ _____ _____ _____	___/_____ ___/_____ ___/_____ ___/_____
HBsAg Test kit:	_____ _____ _____ _____	___/_____ ___/_____ ___/_____ ___/_____
Anti-HCV Test kit:	_____ _____ _____ _____	___/_____ ___/_____ ___/_____ ___/_____
T.pallidum Test kit:	_____ _____ _____ _____	___/_____ ___/_____ ___/_____ ___/_____
Malaria Test kit:	_____ _____ _____ _____	___/_____ ___/_____ ___/_____ ___/_____

Report completed by (please print name): _____ Date ____/____/____

Please return the top (blue) copy of this form along with Section 1 and Section 3 of this month's donation testing report to - The Medical Director (Infection Surveillance), National Blood Authority, Oak House, Reeds Crescent, Watford, WD1 1QH.. See folder front cover for full addresses. Thank you for your help

[Form code: DTS 2 02]

NATIONAL BLOOD SERVICE: DONATION TESTING SURVEILLANCE

SECTION 3: Repeatedly reactive donations & donations for confirmatory testing : c) ANTI-HIV

BTC : _____ Month _____ Year _____ Test (ie.manufacturer) & batch number: _____

Please enter information in the blank spaces provided or **circle one option** in each of the columns with options provided (*some spaces are left for internal use as required*).

Donation number	Donation date	Donor type	Screen results :-				To conf. lab *If yes,*	HIV infection	
		NEW PR-Old:previously reactive NPR-Old:not previously reactive	Initially reactive	*For BTC internal use*	Repeatedly reactive	*For BTC internal use*		Confirmatory lab conclusion (Leave uncircled until conclusion is received ie. do not circle ND=NOT DONE when result is still awaited)	*For BTC internal use*
_____		NEW PR NPR	YES NO		YES NO		YES NO	POS NEG UNDET ND	
_____		NEW PR NPR	YES NO		YES NO		YES NO	POS NEG UNDET ND	
_____		NEW PR NPR	YES NO		YES NO		YES NO	POS NEG UNDET ND	
_____		NEW PR NPR	YES NO		YES NO		YES NO	POS NEG UNDET ND	
_____		NEW PR NPR	YES NO		YES NO		YES NO	POS NEG UNDET ND	
_____		NEW PR NPR	YES NO		YES NO		YES NO	POS NEG UNDET ND	
_____		NEW PR NPR	YES NO		YES NO		YES NO	POS NEG UNDET ND	
_____		NEW PR NPR	YES NO		YES NO		YES NO	POS NEG UNDET ND	
_____		NEW PR NPR	YES NO		YES NO		YES NO	POS NEG UNDET ND	

Top(pink) copy:Please return during the 2nd week following the 4-week period to The Medical Director, (CDSC/NBA Infection Surveillance), National Blood Authority, Oak House, Reeds Crescent, Watford,HERTS. WD1 1QH. Do not delay while awaiting confirmatory test results. Use the second copy to continue recording confirmatory results on these samples.

2nd(pink) copy:Please return to the above address along with the next 4-week's report (top copy) even if some confirmatory test results are still outstanding.

Back(white) copy:Please keep for your own records.

Please continue on another sheet if a different test/batch is used within the period or if space for more records is needed .....

[Form code: DTS 3.01:c]

Report completed by (please print name): _____ Date ____/____/____

Donor: _____

NATIONAL BLOOD SERVICE

INFECTION SURVEILLANCE

INFECTED DONOR SURVEILLANCE

This folder is for recording and reporting information about a donor found to be infected with HBV, HCV (positive or indeterminate test results) , HIV or *T.pallidum* by the National Blood Service. A designated person at your blood centre should be responsible for completing these forms.

Section 1 is for recording the donor, donation, and testing details known at the blood centre at the time when an infection is confirmed. Section 1 should be completed at the blood centre when complete confirmatory test results are received. When Section 1 has been completed please send the top (blue) copy to :

The Medical Director, (Infection Surveillance),
National Blood Authority, Oak House, Reeds Crescent, Watford,
Herts. WD1 1QH

(If a subsequent sample from this donor (ie. a "confirmatory", or "diagnostic" sample) indicates an error in the results of tests on the initial sample please notify the Infection Surveillance Officer who will withdraw the initial report.)

Instruction for reporting HCV RNA (PCR) results **(1/4/99 onwards): Please record the results of PCR tests done at the confirmatory laboratory on a singleton sample by "HCV PCR (Singleton)". Please record, if known, the results of PCR tests done by the NAT laboratory on a pooled sample by "NAT result (If known)". If the donation was not tested by pooled NAT testing, "ND" (not done) should be circled. If the donation was initially detected as HCV infected by NAT testing (i.e. non-reactive to antibody test) please tick the box provided to indicate this, and date the other test results if they relate to samples collected subsequent to the donation.**

Section 2 is for the recording of donor details known only by a clinician, or other carer, who subsequently communicates with the donor about the confirmed infection(s) or who knows the donor as a patient. If the blood centre is undertaking initial follow up of the donor's infection, Section 2 should be completed at the blood centre and the top copy (blue) sent to The Medical Director, NBA (address as above). If the blood centre refers the donor to another carer, please complete the donation and report identity information at the top of Section 2 and then forward Section 2 to the other carer. The carer should then return the completed report to the NBA.

There is no need to complete a separate laboratory report form for PHLS CDSC as information on these reports will be provided by the NBA to the relevant voluntary confidential national surveillance systems, and to local public health doctors.

If you have any questions about the completion of these reports please call CDSC/NBA Infection Surveillance Officer (Kate Soldan), on 0181 200 6868 x4602 or email ksoldan@phls.nhs.uk.

NOTES ON COMPLETING THE FORMS:

1. *Test results*

The following abbreviations are used to describe test results and final confirmatory testing conclusions:

POS	A positive result to a test, or a positive conclusion regarding infection.
NEG	A negative result to a test, or a negative conclusion regarding infection.
EQV	An equivocal result to a test.
ND	A test was not done, or confirmatory testing was not done.
INDET	Confirmatory test results do not conclude that this donation is either positive or negative. The infection status of the donation is concluded as INDETERMINATE. (For HCV see the "Definition of an indeterminate donor for the HCV lookback".)

2. *Soundex coding*

The soundex code of each donors surname is requested as an identifier. No soundex code is unique for a single surname. Mainly because soundex codes ignore vowels, all soundex codes can relate to several names, for example, H-300 is the code for Hutt, Heite, Hyde and Hoade among many possibilities. However, if the soundex code is used in combination with first initial, date of birth and sex, duplicate reports can be identified and reports for an individual can be updated.

Instructions for the manual coding of surnames into soundex codes and a small programme for computer generation of soundex codes have been sent to your blood centre. If these are not accessible at the time of completing a form please contact Kate Soldan (0181 200 6868 x4602), or call the PHLS AIDS Division (0181 200 6868 x4420, 4453, 4406, 4562, 4559) and ask for the soundex code of a surname or list of surnames. If surnames are written in full on to these forms, they will be converted to soundex on receipt at the NBA.

: INFECTED DONOR SURVEILLANCE

CONFIDENTIAL

SECTION 1: Donor & donation information

Please complete this report for each donor with a newly confirmed HIV, HBV, HCV or T.pallidum infection, or with an indeterminate HCV infection. Please write into the spaces provided or tick the appropriate box.

BC where infection was detected *(& PTT case code if applicable)*	Donation number	Donation date
	_ _ _ _ _ _ _ _ _ _ _ _ _ _	___/___/___

Soundex of donor's surname	Initial(s)	Sex	Date of birth	Donor's postcode *exclude end letters*
			___/___/___	_ _ _ _ _ _ _ _

1. Results of confirmatory tests *(please circle/complete the correct results in detail and the final confirmatory conclusion, ND=not done)*:

Infection	*Marker* *result* *by: test used (manufacturer and kit)*	*Final Conf. result*
HIV 1&2	anti-HIV : POS NEG EQV ND by:_____ HIV antibodies(WB): _____ by:_____ Levels: _____ HIV RNA(PCR) : POS NEG EQV ND	HIV1- POS / NEG HIV2- POS / NEG ND
HBV	HBsAg : POS (RPHA titre/iu/ml.....) NEG ND by:_____ Neutralised? YES NO ND anti-HBcIgM : POS NEG EQV ND by:_____ anti-HBc total : POS (%inhib/level.....) NEG ND by:_____ HBeAg : POS NEG ND by:_____ anti-HBe : POS NEG ND by:_____ anti-HBs : POS (level.....miu/ml) NEG ND by:_____	CARRIER / ACUTE NEG / ND
HCV	anti-HCV : POS NEG EQV ND by:_____ HCV antigens: _____ by:_____ Levels/intensities: _____ HCV PCR (Singleton) : POS NEG EQV ND NAT result (If known) : POS NEG ND Please tick box (& date results) if infection initially detected only by NAT testing 10 ☐	POS / NEG INDET / ND
T. pallidum		POS / NEG / ND

Notes:

2. To which ethnic group does the donor consider himself/herself to belong?

White ☐1, Black-Caribbean ☐2, Black-African ☐3, Black-other ☐11, Indian/Pakistani/Bangladeshi ☐12,

Chinese ☐4, Other, Asian ☐7, Other, specify: _____, Not known ☐9,

. i) Does this donor have any previous donations on record ?

at this BC..... yes ☐13, no ☐14, not known ☐15,

to another BC in the UK..... yes ☐16, no ☐17, not known ☐18,

to a non-UK transfusion centre..... yes ☐19, no ☐20, not known ☐21,

ii) If "yes" (ie. donor has donated previously) please give details of the most recent previous donation :

BC of donation	Donation number of most recent previous donation	Donation date
	_ _ _ _ _ _ _ _ _ _ _ _ _ _	___/___/___

iii) What were the test results for this most recent previous donation taken by the blood transfusion service?

Not tested for the infection(s)[1] now detected ..... ☐25,

[1] *If two or more infections, please note infection(s) in the margin beside each tick.*

Non-reactive to the screening test(s) for the infection(s) detected[2] ..... ☐26,

[2] *Please specify test kit used(ie. manufacturer and generation):* _____

Reactive to the screening test(s) & i) confirmed negative[3] ..... ☐27,

ii) result(s) undetermined[3] ..... ☐28,

[3] *Please specify confirmatory tests and results:* _____

Confirmed positive..... ☐29,

Tested at another BC, result not known at this BC ..... ☐30,

Results not known/not traceable ..... ☐31,

iv) Is an archived specimen available from this previous donation? ..... yes ☐32, no ☐33, not known ☐34,

v) Has this donor ever been an apheresis donor? ..... yes ☐35, no ☐36, not known ☐37,

Report completed by *(please print)*: Date: / /

Please return the top(blue) copy of this form to: The Medical Director, (Infection Surveillance), National Blood Authority, Oak House, Reeds Crescent, Watford, Herts. WD1 1QH.
Thank you for your help. [Form code: IDS 1.02]

CONFIDENTIAL

: INFECTED DONOR SURVEILLANCE

SECTION 2: Donor exposure history for blood borne infections

Please complete this report for each donor with a confirmed HIV, HBV, HCV or T pallidum infection or an indeterminate HCV infection.

BC where infection was detected	Donation number	Donation date
	_ _ _ _ _ _ _ _ _ _ _ _ _ _	___/___/___

Soundex of donor's surname	Initial(s)	Sex	Date of birth
			___/___/___

1. Please tick the appropriate summary of the follow-up of the donor's exposures to infection

a. Donor has no identifiable risk i.e. no risk for infection identified despite satisfactory information provided ..... ☐ 1 } go to Q4

b. Risk for the donor not identified possibly because of incomplete follow-up/information ..... ☐ 2

c. One or more probable risks for infection identified (*please specify all below*) ..... ☐ 3

2. If c. to question 1, please specify probable risks for infection by ticking all that apply, deleting options and describing in free text as appropriate. If ticking "yes" to any exposure, please indicate the country of the exposure (UK or abroad), and the first and last year of the donor's exposure. For donors with multiple exposures please asterisk (*) the exposure which you think is the most probable route of infection.

Donor's probable exposure(s) to blood borne infections	Yes	If Yes ✔	UK	Abroad (please specify country)	First year	Last year
Injecting drug use						
Sex between men (i.e. homosexual intercourse)						
Sex between men and women (i.e. heterosexual intercourse) *please give details of sexual partner(s) risk factor(s) below*						
Blood / tissue / organ recipient *please delete as appropriate*						
Occupational exposure to blood						
Probable perinatal/horizontal exposure in childhood						
Other suspected exposure (eg. household exposure(as adult), renal dialysis, surgical/dental/invasive medical treatment, tattooing, acupuncture, ear and body piercing, blood-sharing) *Please describe*:						

Donor's heterosexual partner(s)	Yes
Has HIV / HBV / HCV / *T.pallidum* *please delete as appropriate*	
Is a man who has had sex with a man (i.e. a homosexual man)	
Is/was an injecting drug user	
Is/was paid for sex	
Has lived in/visited Africa	
Has received blood product treatment (eg.has haemophilia)	
Is a transplant / transfusion recipient *please delete as appropriate*	
Other known exposure, *please describe*:	

Comments:

3. If c. to question 1, do you know why the donor did not disclose an existing risk factor (as detailed above) at the time of donating blood?

No: no reason obtained ☐ 1 Yes: ☐ 2 *please describe the reason*

4. To which ethnic group does the donor consider himself/herself to belong?

White ☐ 1 Black-Caribbean ☐ 2 Black-African ☐ 3 Black-other ☐ 4 Indian/Pakistani/Bangladeshi ☐ 5

Chinese ☐ 6 Other, Asian ☐ 7 Other, specify: _____ 8 Not known ☐ 9

5. In which country was this donor born ? _____

6. Does this donor say he/she has ever donated blood prior to the date above? ..... yes ☐ 1 no ☐ 2 not known ☐ 9

If "yes", please give details of the most recent previous donation:

Country/BC	Donation date
	___/___/___

7. Has this donor had any clinical signs of this(/these) infection(s)? ..... yes ☐ 1 no ☐ 2 not known ☐ 9

If "yes", please describe with dates:

Report completed by (*please print*): Date: / /

Please return the top(blue) copy of this form to: The Medical Director, (Infection Surveillance), National Blood Authority, Oak House, Reeds Crescent, Watford, Herts. WD1 1QH
Thank you for your help

[Form code: IDS 2 02]

PHLS NATIONAL BLOOD SERVICE 1

PTI case code: [ ] 1

NATIONAL BLOOD SERVICE

INFECTION SURVEILLANCE

POST-TRANSFUSION INFECTION SURVEILLANCE *(NON-BACTERIAL)*

Please use the enclosed forms to report all (non-bacterial) infections (including HAV, HBC, HCV, HIV, & parasitic infections) in transfusion recipients about which you are informed*, and to report a summary of your investigations of implicated units.

A designated person at your blood centre should be responsible for completing these forms.

Section 1 (PTI case report) is for reporting each infection in a transfusion recipient which you are informed about which meets the following criteria*:

A. i) the receipt of transfusion has been confirmed, **and**
ii) the infection has been confirmed (by detection of antibody, antigen, RNA/DNA etc.), **and**
iii) there is no evidence that the recipient was infected prior to transfusion,

or B. i) **and** iv) the recipient has acute clinical hepatitis of no known cause (ie. including no evidence of acute HAV, HBV, HCV, EBV or CMV infection in post-transfusion samples to date)

(An infection satisfying these criteria will be referred to as a post-transfusion infection (PTI) case.)

* *Except* HCV infected recipients transfused prior to September 1991 with blood not tested for HCV antibodies.

Some PTI cases will lead to an investigation of the donation(s) and donor(s) of the recipient's transfusion(s); some will not: please record this at the bottom of Section 1. Please complete a Section 1 form as soon as possible after you are informed of an infection in a transfusion recipient and send the top copy (yellow) to:-
The Medical Director, National Blood Authority, Oak House, Reeds Crescent, Watford, Herts. WD1 1QH

Please keep the back (white) copy for your own records.

Section 2 (PTI donor/donation investigation report) and Section 3 (PTI conclusion of investigation) are for reporting the outcome of any investigation of implicated units. If all the units implicated in the PTI case were produced by your blood centre, a Section 2 & 3 form should be attached to the PTI case file for completion, and posting (top copies only) to The Medical Director, NBA (at the address above) when the investigation is closed.
If one or more unit(s) implicated in the case were produced by one or more other blood centre(s), copies of Section 2 & 3 should be sent to each relevant blood centre(s) along with the details of their implicated unit(s). (A photocopy of the Section 1 form may also be sent as a summary of the case details.) After investigation of the implicated unit(s), the other blood centre(s) should complete Section 2 and Section 3 parts A & B and return the top copies to the blood centre who initiated the PTI case investigation. The date of completion of Section 3 will be taken as the date on which the investigation was closed. The case-initiating blood centre should complete a Section 2 and a Section 3, parts A, B, **and C**, and send the top copies, along with photocopies of the Section 2 & 3 reports from other blood centres relating to the case, to The Medical Director, NBA.

Please prefix your own unique number/code for the PTI case with the first three letters of your blood centre name when recording the `PTI case code' on each form. This will enable each case reported to be clearly identified, and will also allow linkage of Section 1 and Section 2 & 3 reports. It is therefore particularly important to enter this case code on to each Section 2 & 3 form before sending to any other blood centre(s) who produced units implicated in the same case.

continued overleaf...

If a donor is found by a PTI investigation to have markers of infection with HBV, HCV, HIV or *T.pallidum*, please complete an **Infected Donor Surveillance** report (Sections 1&2). Please complete these forms for the donation which was implicated by the investigation ie. the donation which is believed to have transmitted an infection, even if this donation has no markers of infection, and write the PTI case code next to your blood centre name on Section 1 of the Infected Donor Surveillance report. (The Infected Donor Surveillance reports are not suitable for collecting information about donors found to have markers of other transfusion transmissible infections and information about such cases may be requested by other means as appropriate.) *(See back cover for reporting summary.)*

If a look-back at other recipients of an infected donor discovers additional post-transfusion infection(s), please report each PTI on a separate set of forms: please record the blood centre as the source of the report, and "look-back after (PTI case code)" as the reason for diagnosis on Section 1.

Test results

The following abbreviations are used to describe test results:

POS	A positive result to a test.
NEG	A negative result to a test.
EQV	An equivocal result to a test.
ND	A test was not done.

Soundex coding

The soundex code of each donors surname may be used instead of surname as an identifier. No soundex code is unique for a single surname. Mainly because soundex codes ignore vowels, all soundex codes can relate to several names, for example, H-300 is the code for Hutt, Heite, Hyde and Hoade among many possibilities. However, if the soundex code is used in combination with first initial, date of birth and sex, duplicate reports can be identified and reports for an individual can be updated.

Instructions for the manual coding of surnames into soundex codes and a small programme for computer generation of soundex codes have been sent to your blood centre. If these are not accessible at the time of completing a form please contact Kate Soldan (0181 200 6868 x4602), or call the PHLS AIDS Division on 0181 200 6868 x4420, 4453, 4406, 4562, 4559 and ask for the soundex code of a surname or list of surnames. If surnames are written in full on to these forms, they will be converted to soundex on receipt at the NBA.

Example Section 2 question 2

2. Infection status of the donor(s)

Please record the results of re-testing the implicated donation(s)/donor(s) in the table below. Use one line to summarise all similar tests ie. the same test(s) and same result(s) on a similar specimen type. Please record re-tests on **archived** samples (and pack residues) from the implicated donation(s) and re-tests on **subsequent** samples (which may be *either* fresh *or* archived subsequent donations, *or* specially bled fresh samples) from the implicated donors separately. Record results by writing **POS, NEG, EQV** (equivocal) and/or the titre/level in each column. An empty cell will be taken as indication that the test was not performed.

For a post-transfusion HBV case, with implicated donations from 13 donors, the summary testing results could look like this :-

	Number and type of samples (ARCHIVE/SUB.SAMPLE)	HAV	HBV					
		anti-HAV IgM	HBsAg	anti-HBc (total)	anti-HBc IgM	HBeAg	anti-HBe	anti-HBs
1.	[ ]2 x							
2.	[ ]3 x							
3.	[ ]4 x							
4.	[ ]5 x							
5.	[ ]6 x							
6.	[ ]7 x							

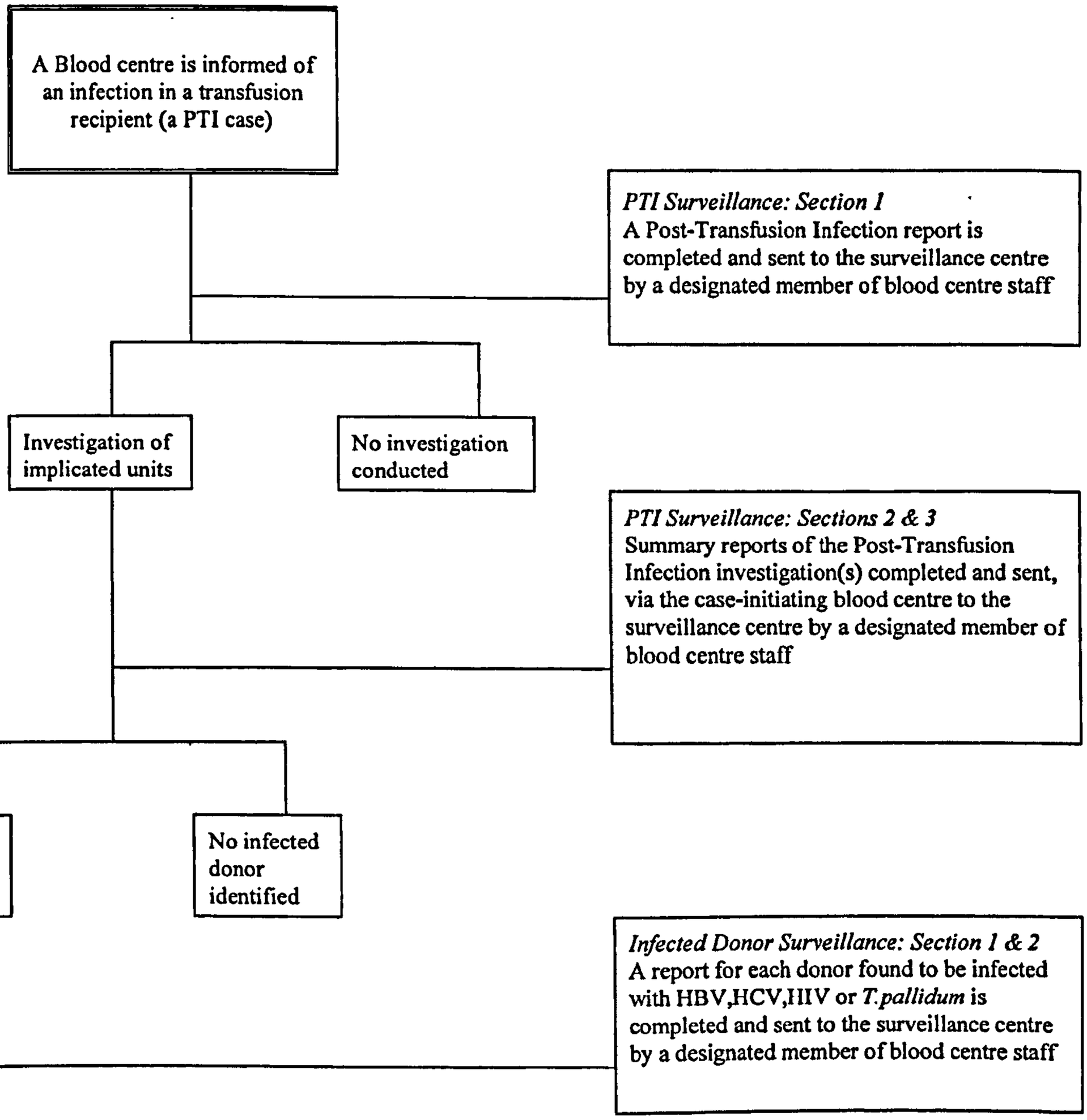
ie. all archives were re-tested, 8 donors provided a subsequent sample, one donor was anti-HBc positive, with no anti-HBs.

The conclusions for this investigation (Section 3, part A) would therefore include :-

B. ____8 donor(s) was(were) found through re-testing of archive samples to have markers of transmissible infection .....[ ]9,
Please specify the implicated unit type(s):_____

If you have any questions about the completion of these reports please call Kate Soldan, NBA/CDSC Infection Surveillance Officer, on 0181 200 6868 x4602

Summary of surveillance reports for a PTI case



[1] If other donations(s) from the infected donor(s) are investigated, ie. a look-back at other recipients is conducted, a Post-Transfusion Infection report (Sections 1,2 & 3) should be completed for each recipient who satisfies the criteria for a post-transfusion infection (see front of folder for criteria of a PTI).

PHLS NATIONAL BLOOD SERVICE 2

PTI case code: [ ] 10

NATIONAL BLOOD SERVICE

INFECTION SURVEILLANCE

POST-TRANSFUSION INFECTION SURVEILLANCE *(BACTERIAL)*

Please use the enclosed forms to report all bacterial infections in transfusion recipients, and post-transfusion reactions suspected to be due to bacteria, about which you are informed, and to report a summary of your investigations of implicated units.

A designated person at your blood centre should be responsible for completing these forms.

Section 1 (PTI case report) is for reporting each infection/reaction in a transfusion recipient which you are informed about which meets the following criteria*:

A. i) the receipt of transfusion has been confirmed, **and**
ii) the infection has been confirmed, **and**
iii) there is no evidence that the recipient was infected prior to transfusion,

or B. i) **and** iv) the recipient has a post-transfusion reaction suspected (but not confirmed by laboratory tests) to be due to bacteria

(Cases meeting these criteria will be referred to as post-transfusion infections (PTI) and post-transfusion reactions suspected to be due to bacteria (PTR).)

Some PTI/PTR cases will lead to an investigation of the donation(s) and donor(s) of the recipient's transfusion(s); some will not: please record this at the bottom of Section 1. Please complete a Section 1 form as soon as possible after you are informed of an infection/reaction in a transfusion recipient and send the top copy (yellow) to:-

The Medical Director, National Blood Authority, Oak House, Reeds Crescent, Watford, Herts. WD1 1QH

Please keep the back (white) copy for your own records.

Section 2 (donor/donation investigation report) and Section 3 (conclusion of investigation) are for reporting the outcome of any investigation of implicated units. If all the units implicated in the PTI/PTR case were produced by your blood centre, a Section 2 & 3 form should be attached to the PTI/PTR case file for completion, and posting (top copies only) to The Medical Director, NBA (at the address above) when the investigation is closed.

If one or more unit(s) implicated in the case were produced by one or more other blood centre(s), copies of Section 2 & 3 should be sent to each relevant blood centre(s) along with the details of their implicated unit(s). (A photocopy of the Section 1 form may also be sent as a summary of the case details.) After investigation of the implicated unit(s), the other blood centre(s) should complete Section 2 and Section 3 parts A & B and return the top copies to the blood centre who initiated the PTI/PTR case investigation. The date of completion of Section 3 will be taken as the date on which the investigation was closed. The case-initiating blood centre should complete a Section 2 and a Section 3, parts A, B, **and C**, and send the top copies, along with photocopies of the Section 2 & 3 reports from other blood centres relating to the case, to The Medical Director, NBA.

3 : POST-TRANSFUSION INFECTION SURVEILLANCE

CONFIDENTIAL

SECTION 1: Confirmed post-transfusion infection report

Please complete one report for each transfusion recipient **as soon as possible.**

Blood centre to which infection was reported	PTI case code: *(BC prefix)* *(BC case no./code)* ___:_____	Date of 1st report to BC: ___/___/___

Source of report to blood centre(name and institution of notifier)

Recipient's surname or soundex	Initial(s)	Sex	Date of birth ___/___/___

A. PTI information

1. Reason for diagnosis (please tick):

Hepatitis infection

Clinical acute hepatitis ..... ☐ 20 1
Symptomatic chronic liver disease ..... ☐ 21 2
Hepatocellular carcinoma ..... ☐ 22 3
Abnormal liver function: routine testing ..... ☐ 23 4
HAV/HBV/HCV markers: routine testing ..... ☐ 24 5
Other, please specify: 6

HIV infection

HIV related symptoms, not AIDS ..... ☐ 25 7
AIDS ..... ☐ 26 8
HIV markers found on routine testing ..... ☐ 27 9
Other, please specify: 10

Other infection

CMV infection ..... ☐ 28 11
Malaria ..... ☐ 29 12
HTLV infection ..... ☐ 30 13
B19 infection ..... ☐ 31 14
Bacteraemia ..... ☐ 32 15
Specify species if known _____
Post-transfusion reaction (PTR) ..... ☐ 33 16
(suspected, but not confirmed, to be due to bacteria)
Other, please specify: 17

Notes & symptoms :

3. Date of a) onset of symtoms: ___/___/___ **or,** b) diagnosis of sub-clinical infection: ___/___/___

4. Date of latest report of the recipient and status at that time: ___/___/___

Dead, infection implicated ..... ☐ 37 1
Dead, no known involvement of the infection ..... ☐ 38 2
Symptomatic ..... ☐ 39 3
Asymptomatic ..... ☐ 40 4

5. Had the recipient had any other known risk exposures for this infection? ..... yes ☐ 41 1, no ☐ 42 2, not known ☐ 43 3,
(eg. IDU, sexual/household contact with an infected person, surgery, organ/tissue transplant, fractionated blood product treatment, transfusion abroad)

If "yes", please specify:

6. Infection status of the recipient

Please enter the significant test results (ie. pre-transfusion, post-transfusion and follow up as available) for the recipient's samples in the table below. Please enter **POS** (positive), **NEG** (negative) **EQV** (equivocal) and/or the titre/level as appropriate in each box. An empty box will taken as indication that the test was not performed.

	HAV	**HBV**						**HCV**			**HIV**	**Other**	Lab where tests were performed
Specimen date	anti-HAV IgM	HBsAg *(titre)*	anti-HBc (total) *(%anhib/ level)*	anti-HBc IgM	HBeAg	anti-HBe	anti-HBs *(titre)*	anti-HCV ELISA(s)	RIBA	HCV RNA	anti-HIV		
1. ___/___/___													
2. ___/___/___													
3. ___/___/___													

B. Transfusion information

1. Hospital of transfusion: _____

2. Reason for transfusion: _____

3. Date/period over which transfusion(s) was/were given: ___/___/___ to ___/___/___

4. Number and type of units transfused:

red cells	x ☐46	cryoprecipitate	x ☐47
platelets	x ☐48	other	x ☐49
whole blood	x ☐51	not known	x ☐52
FFP	x ☐54		

Total number of units = ☐55 [= ☐56 from this BC + ☐57 from other BCs, specify: _____ _____]

If CMV infection is reported,

4b. How many units were

i) labelled CMV antibody negative ☐50

ii) leucocyte depleted ☐53

5. Based on the available information about the recipient and the implicated donation(s)/donor(s), ie.A&B above, was an investigation of the donation(s)/donors(s) initiated?

Yes ☐58, *please attach Section 2&3report forms to the case's file for completion once the investigation is closed.*

No ☐59, Please state reason: _____ _____

Report completed by *(please print name)*: _____ Date ___/___/___

Please return the top(yellow) copy of this form to.- The Medical Director, (Infection Surveillance) National Blood Authority, Oak House, Reeds Crescent, Watford, Herts., WD1 1QH. Thank you for your help.

[Form code.PTIS 1.02]

Appendix 5

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: POST-TRANSFUSION INFECTION SURVEILLANCE

Section 2 (NON-BACTERIAL): Confirmed post-transfusion infection donor/donation investigation report

Please complete one form for each PTI case investigated by your blood centre.

Investigation of _____ units from _____ blood centre pertaining to the PTI investigation with the case code ___ ___ ___ : _____ _____ _____ _____
(BC prefix) *(BC case no./code)*

A. Donation/donor information

1. Review of test results and QC test results for original testing of implicated donations:

All checked and found correct ..... ☐60, Error found in testing/labelling/issuing procedures, please specify:_____ ☐61, Checking incomplete, ____ of ____ units un-checked ☐62,

2. Infection status of the donor(s)

Please record the results of re-testing the implicated donation(s)/donor(s) in the table below. Use one line to summarise all similar test(s) ie. the same tests and same result(s) on a similar specimen type. Please record re-tests on **archived** samples (and pack residues) from the implicated donations and re-tests on **subsequent** samples (which may be *either* fresh *or* archived subsequent donations, *or* specially bled fresh samples) from the implicated donors separately. Please record results by writing **POS, NEG, EQV** (equivocal) and/or the titre/level (HBsAg, anti-HBc(total) & antiHBs) in each column. An empty cell will be taken as indication that the test was not performed.

	HAV	HBV						HCV			HIV	Other	Lab where tests where performed	Notes
Number and type of samples (ARCHIVE/SUB.SAMPLE)	anti-HAV IgM	HBsAg	anti-HBc (total)	anti-HBc IgM	HBeAg	anti-HBe	anti-HBs	anti-HCV ELISA(s)	anti-HCV RIBA	HCV RNA	anti-HIV			
1. ☐63 x ___														
2. ☐64 x ___														
3. ☐65 x ___														
4. ☐66 x ___														
5. ☐67 x ___														
6. ☐68 x ___														

3. Does any donor have a history which suggests exposure to blood borne infection? (eg. a donor's records note past jaundice) yes ☐69, no ☐70, not known ☐71,

If "yes" please give details, and specify which line(s) of the above table contain this donor's test results:_____

4. Have any of the donors been involved in any other PTI case(s)? yes ☐72, no ☐73, not known ☐74,

If "yes" please specify which line(s) of the above table contain this/these donor(s) and the other PTI case code(s):_____

Report completed by *(please print name)*: _____ Date ____/____/____

Please return the top(yellow) copy of this form to:- The Medical Director (CDSC/NBA Infection Surveillance), National Blood Authority, Oak House, Reeds Crescent, Watford, Herts. WD1 1QH. Thank you for your help. [Form code:PTIS 2.02]


5: POST-TRANSFUSION INFECTION SURVEILLANCE

Section 3 (NON-BACTERIAL): Confirmed PTI investigation summary

Conclusion of investigation

Blood centre	PTI case code: *(BC prefix)* *(BC case no./code)* ___:_____

A. Conclusion of this blood centre's investigation

Please tick your conclusion(s) for the investigation of donation(s)/donor(s) at your blood centre. Please insert the correct number in the space to complete the conclusion where appropriate.

The recipient's infection **was probably** acquired by transfusion with a unit from this blood centre:

A. Errors were found in compliance with SOP(s) in force at the time of testing/labelling/issuing of the implicated unit(s) ..... ☐ 77₁

B. ___78 donor(s) was(were) found through re-testing of archive samples to have markers of transmissible infection ..... ☐ 79₂

Please specify the implicated unit type(s):_____

C. ___80 donor(s) was(were) found through testing of subsequent samples to have markers of transmissible infection ..... ☐ 81₃

Please specify the implicated unit type(s):_____

The recipient's infection **may** have been acquired by transfusion with a unit from this blood centre:

D. For ___82 donor(s) no sample subsequent to the implicated donation was tested ..... ☐ 83₄

E. For ___84 donor(s) no archive sample of the implicated donation was tested ..... ☐ 85₅

F. For ___86 donor(s) neither an archive sample of the implicated donation, nor a subsequent sample was tested ..... ☐ 87₆

The recipient's infection **was probably not** acquired from transfusion with a unit from this blood centre:

G. Archived samples or subsequent samples were obtained from **all** donors; none were found to have markers indicative of possible infectivity at the time of donating the implicated unit(s) ..... ☐ 88₇

H. Other e.g. the blood centre has been informed of another confirmed source of the recipient's infection ..... ☐ 89₈

Please specify:_____

B. Actions of this blood centre as a results of this investigation

Please insert the correct number in the box to indicate the outcome of this investigation for the donor(s) involved.

A. ___90 donor(s) was(were) removed from the panel because confirmed markers of TTI were found in their blood.

B. ___91 donor(s) was(were) removed from the panel because of repeated involvement in PTI case investigations.
(Other PTI case code(s):_____, _____,_____)

C. ___92 donor(s) was(were) flagged/marked on the donor database as having been involved in a PTI case investigation.

D. ___93 other donation(s) from the infected donor(s) are being investigated ie. look-back at recipients is being conducted.

Please describe any other actions following this investigation: _____

C. Conclusion of case investigation

The recipient's infection **was probably** acquired by transfusion with a unit from the blood service:

A. Errors were found in compliance with SOP(s) in force at the time of testing/labelling/issuing of the implicated unit(s) ..... ☐ 94₁

B. ___95 donor(s) was(were) found through re-testing of archive samples to have markers of transmissible infection ..... ☐ 96₂

C. ___97 donor(s) was(were) found through testing of subsequent samples to have markers of transmissible infection ..... ☐ 98₃

If B or C is true:

Please specify the implicated unit type(s):_____

Please specify the implicated DONOR type: NEW ☐, REPEAT ☐ - Date of previous donation:___/___/___

Please give the date the recipient was transfused with this unit: ___/___/___

The recipient's infection **may** have been acquired by transfusion with a unit from the blood service:

D. For ___99 donor(s) no sample subsequent to the implicated donation was tested ..... ☐ 100₄

E. For ___101 donor(s) no archive sample of the implicated donation was tested ..... ☐ 102₅

F. For ___103 donor(s) neither an archive sample of the implicated donation, nor a subsequent sample was tested ..... ☐ 104₆

The recipient's infection **was probably not** acquired from transfusion with a unit from the blood service:

G. Archived samples or subsequent samples were obtained from **all** donors; none were found to have markers indicative of possible infectivity at the time of donating the implicated unit(s) ..... ☐ 105₇

H. Other e.g. the blood service has been informed of another confirmed source of the recipient's infection ..... ☐ 106₈

Please specify:_____

NB. Please also complete IDS forms for any HIV/HBV/HCV infected donors detected by this investigation.

Report completed by *(please print name)*: _____ Date ___/___/___

Please return the top(yellow) copy of this form to:- The Medical Director (CDSC/NBA Infection Surveillance), National Blood Authority, Oak House, Reeds Crescent, Watford, Herts. WD1 1QH. Thank you for your help. [Form code:PTIS 3.02]

6: POST-TRANSFUSION INFECTION SURVEILLANCE

Section 2 (BACTERIAL): PTI or PTR donor/donation investigation report

Please complete one form for each PTI case investigated by your blood centre.

Investigation of _____ units from _____ blood centre pertaining to the PTI investigation with the case code _____ : _____
(BC prefix) *(BC case no./code)*

A. Investigation details

1. Samples were obtained from:
The implicated component: ☐107,
Other components from the implicated donation: ☐108,
please specify: _____
The recipient: ☐109, please specify: _____
The donor: ☐4 please specify: _____
Other: ☐5 please specify: _____

2. Evidence of bacterial infection
Please record the investigations performed and the findings of these investigations

Sample source and type	Investigations performed	Findings

3. Does any implicated donor have a history which may be relevant to the investigation ? (e.g. bacterial illness, skin condition at site of venepuncture for blood donation)?yes ☐110, no ☐111, not known ☐112,
If "yes" please give details: _____

4. Have any implicated donors been involved in any other PTI(bacterial) case(s)? ..... yes ☐113, no ☐114, not known ☐115,
If "yes" please give details: _____

5. Any other information/comments:

Report completed by *(please print name)*: _____ Date ____/____/____

7: POST-TRANSFUSION INFECTION SURVEILLANCE

Section 3 (BACTERIAL): PTI or PTR infection investigation summary

Blood centre	PTI case code: *(BC prefix)* *(BC case no./code)* ___ : _____

A. Conclusion *(please complete for all cases)*

Please tick your conclusion(s) for the investigation of this case (A, B C or D), and as many of the statements I - V that are true.

4

	A. The recipient's transfusion reaction **was probably** caused by bacteria/bacterial toxins from a transfusion of a blood component from the NBS
	B. The recipient's transfusion reaction **may or may not** have been caused by bacteria/bacterial toxins from a transfusion of a blood component from the NBS
	C. The recipient's transfusion reaction **was not probably** caused by bacteria/bacterial toxins from a transfusion of a blood component from the NBS.
	D. Other: *please specify*

I. The recipient was found to have evidence of bacterial infection likely to have caused their transfusion reaction..... ☐118,

II. The implicated component was found to have evidence of bacterial infection..... ☐119,

III. Other components from the implicated donation were found to have evidence of bacterial infection ..... ☐120,
Please specify the component(s):_____

IV. An implicated donor was found to have evidence of bacterial infection likely to have been transmitted by transfusion ..... ☐121,

V. The recipient's reaction was probably caused by bacteria from another source..... ☐122,
Please specify the suspected source:.....Venepuncture site?.....No(unlikely).☐....Possible..☐123....Probable.☐

Other?_____
Note

B. Summary details of implicated agent and component *(please complete unless transfusion has been shown not to be the cause of the recipients reaction)*

1. Bacteria/toxin found, or suspected, to have caused the transfusion reaction: _____
Bacterial load (if known): _____

2. Component type found, or suspected, to have caused the transfusion reaction: _____

If RED CELLS please give details:
Buffy coat depleted?.....YES / NO Leucocyte depleted?.....YES / NO If yes, where? Blood centre ☐124
Bedside ☐125

If PLATELETS please give details:
Recovered ☐126
Apheresis ☐127 If apheresis, please specify collection apparatus: Cobe ☐
Haemonetics ☐
Other *(specify)* ☐ _____
Not known ☐

Pooled?.....YES / NO Leucocyte depleted?.....YES / NO If yes, where? Blood centre ☐128
Bedside ☐129

3. Age of the unit (days) at time of transfusion ☐ 4. Volume transfused: ☐

C. Actions of this blood centre as a results of this investigation

Please insert the correct number in the box to indicate the outcome of this investigation for the donor(s) involved.

A. ____130 donor(s) was(were) removed from the panel because transfusion transmissible infection(s) may be present in their donations / because of repeated involvement in PTI case investigations *(please delete as applicable)*.
(Other PTI case code(s):_____, _____,_____)

B. ____131 donor(s) was(were) flagged/marked on the donor database as having been involved in a PTI case investigation.

C. ____132 other donation(s) are being investigated.

Other actions following this investigation / notes: _____

Report completed by *(please print name)*: _____ Date ____/____/____
(ie. date investigation was closed by your BC)

Please return the top(yellow) copy of this form to:- The Medical Director (CDSC/NBA Infection Surveillance), National Blood Authority, Oak House, Reeds Crescent, Watford, Herts. WD1 1QH. Thank you for your help. [Form code PTIS(bac)
3 02]

NATIONAL BLOOD SERVICE

INFECTION SURVEILLANCE

MONTHLY DONATION TESTING REPORT

For PhD:

SEPTEMBER 1999

i.e September's report Tables 1a&1b,
October's report Tables 2a,1c&2b

Manufacturers' details and centre details removed.

If you have any queries relating to the data in Table 1a, 1b or 1c please contact Alan Slopecki (NBA Head of Quality Assurance: 01277 306000). If you have any queries relating to the data in Table 2a or Table 2b please contact Kate Soldan (NBA/PHLS-CDSC Infection Surveillance Officer: 020 8200 6868 Extn. 4602). The data in Tables 1a-2b Scotland were collated by Dr Brian Dow, SNBTS Microbiology Reference Unit, 0141 357 7708.

CONTENTS

NOTES

Tables 1a and 2a contain data for the most recent month available.
Tables 1b, 1c and 2b contain cumulative data up to the most recent month available.
Tables 1 (a, b and c) present data for monitoring test kit and test kit batch performance.
Tables 2 (a and b) present data for monitoring donor infection rates.

Cumulative tables contain data about donation tested since 1st October 1995 by blood centres in England, Wales, Northern Ireland, the Channel Isles, the Isle of Man and the Republic of Ireland, and since 1st April 1996 by blood centres in Scotland.

PR – previously reactive known donor. NPR – not previously reactive known donor.

The data in the Scottish tables were collected and collated in Scotland and are presented in separate tables.

*** second page is for comparable data from Scotland – not included in PhD.**

HEPATITIS B

Table 1a: HBsAg testing of blood donation [1]: test kit and test kit batch specific results by centre

Donations collected in September 1999

Blood Centre	Test kit	Batch	Number Tested [2]	Number reactive Initially	(%)	Number reactive Repeatedly	(%)	Confirmatory test results [3] Positive	Negative	Undet.	Pending
England			208682	1200	(0.58)	205	(0.10)	10	191	3	0
			16113	67	(0.42)	14	(0.09)	0	12	1	0
			7569	31	(0.41)	11	(0.15)	0	11	0	0
			7633	59	(0.77)	3	(0.04)	0	3	0	0
			15575	74	(0.48)	19	(0.12)	1	18	0	0
			12059	174	(1.44)	23	(0.19)	0	23	0	0
			13439	125	(0.93)	17	(0.13)	1	15	1	0
			14625	39	(0.27)	17	(0.12)	2	14	1	0
			20897	5	(0.02)	3	(0.01)	1	2	0	0
			4920	1	(0.02)	0	(0.00)	0	0	0	0
			2235	33	(1.48)	9	(0.40)	0	9	0	0
			10542	37	(0.35)	16	(0.15)	0	16	0	0
			14238	126	(0.88)	15	(0.11)	2	13	0	0
			7766	35	(0.45)	8	(0.10)	1	7	0	0
			1641	9	(0.55)	1	(0.06)	0	1	0	0
			26365	230	(0.87)	21	(0.08)	0	21	0	0
			4807	16	(0.33)	1	(0.02)	0	1	0	0
			7594	65	(0.86)	6	(0.08)	1	5	0	0
			9994	46	(0.46)	12	(0.12)	0	12	0	0
			10670	28	(0.26)	9	(0.08)	1	8	0	0
Wales			10159	4	(0.04)	2	(0.02)	1	1	0	0
			10159	4	(0.04)	2	(0.02)	1	1	0	0
Northern Ireland			6016	19	(0.32)	1	(0.02)	0	1	0	0
			3303	19	(0.58)	1	(0.03)	0	1	0	0
			2713	0	(0.00)	0	(0.00)	0	0	0	0
Channel Isles & Isle of Man			696	2	(0.29)	1	(0.14)	0	1	0	0
			185	1	(0.54)	1	(0.54)	0	1	0	0
			44	0	(0.00)	0	(0.00)	0	0	0	0
			227	0	(0.00)	0	(0.00)	0	0	0	0
			240	1	(0.42)	0	(0.00)	0	0	0	0
Republic of Ireland			11774	1	(0.01)	0	(0.00)	0	0	0	0
			3240	0	(0.00)	0	(0.00)	0	0	0	0
			8534	1	(0.01)	0	(0.00)	0	0	0	0
Total			237327	1226	(0.52)	209	(0.09)	11	194	3	0

1. Excluding donations from donors being monitored because of previously reactive, but not confirmed to be positive, donations. Details of test results for these donors will be given in the appropriately dated table 2a (third column).

2. Note that the number of test results that are excluded from tables 1a and 1b because they are on donations collected from donors being monitored for previous reactivity to the screening tests is different for each infection. Minor discrepancies between the number of donations tested (by test kit batch) in Tables 1a/b and the number of donations tested (by new and known donor type) in Table 2a may arise for several centres which obtain the denominator counts for these tables from different sources.

3. Discrepancy between the number of donations found to be repeatedly reactive and the sum of positive, negative, undetermined and pending confirmatory results may arise due to referral for confirmatory testing of donations with screening results in the "grey zone".

HEPATITIS C

Table 1a: Anti-HCV testing of blood donations[1]: test kit and test kit batch specific results by centre

Donations collected in September 1999

Blood centre	Test kit	Batch	Number[2] Tested	Number reactive (%) Initially		Repeatedly[3]		Confirmatory test results[4] Positive	Negative	Undet.	Pending
England			208684	297	(0.14)	151	(0.07)	17	101	32	1
			23677	36	(0.15)	14	(0.06)	0	10	4	0
			23205	34	(0.15)	21	(0.09)	0	20	1	0
			25506	32	(0.13)	19	(0.07)	1	1	16	1
			1362	0	(0.00)	0	(0.00)	0	0	0	0
			13268	6	(0.05)	5	(0.04)	1	3	1	0
			20867	19	(0.09)	14	(0.07)	8	6	0	0
			4912	1	(0.02)	1	(0.02)	0	0	1	0
			8999	3	(0.03)	3	(0.03)	0	3	0	0
			3776	5	(0.13)	2	(0.05)	0	2	0	0
			21994	62	(0.28)	30	(0.14)	4	21	5	0
			28040	62	(0.22)	20	(0.07)	2	18	0	0
			12402	22	(0.18)	13	(0.10)	0	11	2	0
			13479	9	(0.07)	5	(0.04)	0	4	1	0
			7197	6	(0.08)	4	(0.06)	1	2	1	0
Wales			10145	10	(0.10)	9	(0.09)	0	7	2	0
			4223	8	(0.19)	7	(0.17)	0	5	2	0
			5922	2	(0.03)	2	(0.03)	0	2	0	0
Northern Ireland			6015	8	(0.13)	4	(0.07)	0	3	1	0
			2708	2	(0.07)	1	(0.04)	0	1	0	0
			3307	6	(0.18)	3	(0.09)	0	2	1	0
Channel Isles & Isle of Man			696	3	(0.43)	2	(0.29)	0	3	0	0
			229	1	(0.44)	0	(0.00)	0	1	0	0
			146	1	(0.68)	1	(0.68)	0	1	0	0
			81	0	(0.00)	0	(0.00)	0	0	0	0
			240	1	(0.42)	1	(0.42)	0	1	0	0
Republic of Ireland			11773	9	(0.08)	8	(0.07)	1	6	1	0
			3240	1	(0.03)	1	(0.03)	0	1	0	0
			8533	8	(0.09)	7	(0.08)	1	5	1	0
Total			237313	327	(0.14)	174	(0.07)	18	120	36	1

1. Excluding donations from donors being monitored because of previously reactive, but not confirmed to be positive, donations. Details of test results for these donors will be given in the appropriately dated table 2a (third column).

2. Note that the number of test results that are excluded from tables 1a and 1b because they are on donations collected from donors being monitored for previous reactivity to the screening tests is different for each infection. Minor discrepancies between the number of donations tested (by test kit batch) in Tables 1a/b and the number of donations tested (by new and known donor type) in Table 2a may arise for several centres which obtain the denominator counts for these tables from different sources.

3. At some blood centres an alternative test kit is used for the repeat testing of donations from donors who have had at least two previous donations, which were at least six months apart, sent for confirmatory testing and found to have no confirmed markers of HCV infection. The repeat testing results, using the alternative test kit, are not shown.

4. Discrepancy between the number of donations found to be repeatedly reactive and the sum of positive, negative, undetermined and pending confirmatory results may arise due to referral for confirmatory testing of donations with screening results in the "grey zone".

HIV

Table 1a: Anti-HIV testing of blood donations[1]: test kit and test kit batch specific results by centre

Donations collected in September 1999

Blood centre	Test kit	Batch	Number[2] Tested	Number reactive (%) Initially		Repeatedly		Confirmatory test results[3] Positive	Negative	Undet.	Pending
England			208720	244	(0.12)	132	(0.06)	0	132	0	0
			2206	1	(0.05)	1	(0.05)	0	1	0	0
			20485	15	(0.07)	12	(0.06)	0	12	0	0
			994	0	(0.00)	0	(0.00)	0	0	0	0
			6695	4	(0.06)	1	(0.01)	0	1	0	0
			7300	7	(0.10)	1	(0.01)	0	1	0	0
			9215	10	(0.11)	9	(0.10)	0	9	0	0
			15455	13	(0.08)	7	(0.05)	0	7	0	0
			10054	10	(0.10)	10	(0.10)	0	10	0	0
			10710	16	(0.15)	2	(0.02)	0	2	0	0
			3920	7	(0.18)	2	(0.05)	0	2	0	0
			20878	17	(0.08)	5	(0.02)	0	5	0	0
			4909	5	(0.10)	1	(0.02)	0	1	0	0
			8395	15	(0.18)	12	(0.14)	0	12	0	0
			4370	2	(0.05)	2	(0.05)	0	2	0	0
			7521	21	(0.28)	20	(0.27)	0	20	0	0
			3807	5	(0.13)	3	(0.08)	0	3	0	0
			3909	1	(0.03)	1	(0.03)	0	1	0	0
			6772	12	(0.18)	6	(0.09)	0	6	0	0
			11924	36	(0.30)	10	(0.08)	0	10	0	0
			16121	27	(0.17)	14	(0.09)	0	14	0	0
			8925	5	(0.06)	4	(0.04)	0	4	0	0
			1379	1	(0.07)	0	(0.00)	0	0	0	0
			2105	0	(0.00)	0	(0.00)	0	0	0	0
			20671	14	(0.07)	9	(0.04)	0	9	0	0
Wales			10144	12	(0.12)	8	(0.08)	0	8	0	0
			10144	12	(0.12)	8	(0.08)	0	8	0	0
Northern Ireland			6026	4	(0.07)	3	(0.05)	0	3	0	0
			6026	4	(0.07)	3	(0.05)	0	3	0	0
Channel Isles & Isle of Man			696	3	(0.43)	2	(0.29)	0	2	0	1
			25	0	(0.00)	0	(0.00)	0	0	0	0
			158	2	(1.27)	1	(0.63)	0	1	0	1
			46	0	(0.00)	0	(0.00)	0	0	0	0
			227	0	(0.00)	0	(0.00)	0	0	0	0
			240	1	(0.42)	1	(0.42)	0	1	0	0
Republic of Ireland			11773	9	(0.08)	6	(0.05)	0	6	0	0
			3240	0	(0.00)	0	(0.00)	0	0	0	0
			7211	9	(0.12)	6	(0.08)	0	6	0	0
			1322	0	(0.00)	0	(0.00)	0	0	0	0
Total			237359	272	(0.11)	151	(0.06)	0	151	0	1

1. Excluding donations from donors being monitored because of previously reactive, but not confirmed to be positive, donations. Details of test results for these donors will be given in the appropriately dated Table 2a (third column).

2. Note that the number of test results that are excluded from tables 1a and 1b because they are on donations collected from donors being monitored for previous reactivity to the screening tests is different for each infection. Minor discrepancies between the number of donations tested (by test kit batch) in Tables 1a/b and the number of donations tested (by new and known donor type) in Table 2a may arise for several centres which obtain the denominator counts for these tables from different sources.

3. Discrepancy between the number of donations found to be repeatedly reactive and the sum of positive, negative, undetermined and pending confirmatory results may arise due to referral for confirmatory testing of donations with screening results in the "grey zone".

T. PALLIDUM

Table 1a: *T. pallidum* testing of blood donations[1] : test kit and test kit batch specific results by centre

Donations collected in September 1999

Blood centre	Test kit	Batch	Number Tested[2]	Number reactive (%) Initially		Repeatedly		Confirmatory test results[3] Positive	Negative	Undet.	Pending
England			208789	275	(0.13)	67	(0.03)	6	57	3	0
			1011	2	(0.20)	0	(0.00)	0	0	0	0
			10691	8	(0.07)	3	(0.03)	0	3	0	0
			7692	3	(0.04)	0	(0.00)	0	0	0	0
			4304	4	(0.09)	2	(0.05)	0	2	0	0
			13459	9	(0.07)	2	(0.01)	0	2	0	0
			9761	21	(0.22)	4	(0.04)	0	4	0	0
			25511	32	(0.13)	8	(0.03)	1	4	2	0
			8646	44	(0.51)	11	(0.13)	0	11	0	0
			5982	8	(0.13)	5	(0.08)	0	5	0	0
			25810	30	(0.12)	8	(0.03)	1	6	1	0
			12780	8	(0.06)	4	(0.03)	0	4	0	0
			4293	27	(0.63)	1	(0.02)	0	1	0	0
			17715	45	(0.25)	4	(0.02)	1	3	0	0
			28043	21	(0.07)	9	(0.03)	0	9	0	0
			1379	0	(0.00)	0	(0.00)	0	0	0	0
			8926	4	(0.04)	2	(0.02)	2	0	0	0
			2105	0	(0.00)	0	(0.00)	0	0	0	0
			16418	5	(0.03)	4	(0.02)	1	3	0	0
			4263	4	(0.09)	0	(0.00)	0	0	0	0
Wales			10156	14	(0.14)	8	(0.08)	0	7	2	0
			8117	11	(0.14)	7	(0.09)	0	5	2	0
			2039	3	(0.15)	1	(0.05)	0	2	0	0
Northern Ireland			6024	10	(0.17)	1	(0.02)	0	1	0	0
			834	0	(0.00)	0	(0.00)	0	0	0	0
			5190	10	(0.19)	1	(0.02)	0	1	0	0
Channel Isles & Isle of Man			696	0	(0.00)	0	(0.00)	0	0	0	0
			229	0	(0.00)	0	(0.00)	0	0	0	0
			227	0	(0.00)	0	(0.00)	0	0	0	0
			20	0	(0.00)	0	(0.00)	0	0	0	0
			220	0	(0.00)	0	(0.00)	0	0	0	0
Republic of Ireland			11774	18	(0.15)	3	(0.03)	1	2	0	0
			3240	4	(0.12)	1	(0.03)	0	1	0	0
			5047	1	(0.02)	0	(0.00)	0	0	0	0
			3487	13	(0.37)	2	(0.06)	1	1	0	0
Total			237439	317	(0.13)	79	(0.03)	7	67	5	0

1. Excluding donations from donors being monitored because of previously reactive, but not confirmed to be positive, donations. Details of test results for these donors will be given in the appropriately dated table 2a (third column).

2. Note that the number of test results that are excluded from tables 1a and 1b because they are on donations collected from donors being monitored for previous reactivity to the screening tests is different for each infection. Minor discrepancies between the number of donations tested (by test kit batch) in Tables 1a/b and the number of donations tested (by new and known donor type) in Table 2a may arise for several centres which obtain the denominator counts for these tables from different sources.

3. Discrepancy between the number of donations found to be repeatedly reactive and the sum of positive, negative, undetermined and pending confirmatory results may arise due to referral for confirmatory testing of donations with screening results in the "grey zone".

HEPATITIS B

Table 2a: HBV infection in blood donor : donor type specific infection rates by centre

Donations collected in September 1999

Blood centre	Donations (cf. table 1a September 1999 report) from New Donors [3] Number tested	Number repeatedly reactive (%)	Number confirmed positive [2]	Donations (cf. table 1a September 1999 report) from Known Donors Number tested	Number repeatedly reactive (%)	Number confirmed positive	Donors being monitored [1] Number tested	Number repeatedly reactive (%)	Number confirmed positive
England									
	20041	38 (0.19)	9	188671	167 (0.09)	1	201	70 (34.83)	0
	2622	2 (0.08)	0	21060	23 (0.11)	0	20	7 (35.00)	0
	2295	4 (0.17)	1	20943	18 (0.09)	0	24	9 (37.50)	0
	3158	8 (0.25)	1	22340	32 (0.14)	0	30	13 (43.33)	0
	981	7 (0.71)	1	13644	10 (0.07)	1	11	6 (54.55)	0
	2258	1 (0.04)	1	23559	2 (0.01)	0	4	1 (25.00)	0
	1279	2 (0.16)	0	11498	23 (0.20)	0	3	3 (100.00)	0
	2141	6 (0.28)	3	19863	17 (0.09)	0	18	4 (22.22)	0
	2450	1 (0.04)	0	25556	21 (0.08)	0	58	11 (18.97)	0
	1260	3 (0.24)	1	11141	4 (0.04)	0	13	4 (30.77)	0
	1597	4 (0.25)	1	19067	17 (0.09)	0	20	12 (60.00)	0
Wales									
	1457	1 (0.07)	1	8702	1 (0.01)	0	2	0 (0.00)	0
	1457	1 (0.07)	1	8702	1 (0.01)	0	2	0 (0.00)	0
Northern Ireland									
	605	0 (0.00)	0	5411	0 (0.00)	0	12	4 (33.33)	0
	605	0 (0.00)	0	5411	0 (0.00)	0	12	4 (33.33)	0
Channel Isles & Isle of Man									
	49	0 (0.00)	0	659	1 (0.15)	0	0	0 (-)	0
	17	0 (0.00)	0	212	1 (0.47)	0	0	0 (-)	0
	20	0 (0.00)	0	207	0 (0.00)	0	0	0 (-)	0
	12	0 (0.00)	0	240	0 (0.00)	0	0	0 (-)	0
Republic of Ireland									
	1406	0 (0.00)	0	10368	0 (0.00)	0	0	0 (-)	0
	308	0 (0.00)	0	2932	0 (0.00)	0	0	0 (-)	0
	1098	0 (0.00)	0	7436	0 (0.00)	0	0	0 (-)	0
Total	23558	39 (0.17)	10	213811	169 (0.08)	1	215	74 (34.42)	0
Frequency of confirmed positive		1 in 2356							

1. Donors being monitored because of previously reactive, but not confirmed positive, donations.

2. More information about confirmed positive infections in blood donors will be reported in a quarterly surveillance report.

3. Guernsey and Jersey blood centres collect samples for testing, but do not collect donations, from "new donors".

HEPATITIS C

Table 2a: HCV infection in blood donor : donor type specific infection rates by centre

Donations collected in September 1999

Blood centre	Donations (cf. table 1a September 1999 report) from New Donors[3]			Donations (cf. table 1a September 1999 report) from Known Donors			Donors being monitored [1]		
	Number tested	Number repeatedly reactive (%)	Number[2] confirmed positive	Number tested	Number repeatedly reactive (%)	Number[2] confirmed positive	Number tested	Number repeatedly reactive (%)	Number[2] confirmed positive
England									
	20041	56 (0.28)	15	188673	95 (0.05)	2	199	116 (58.29)	1
	2622	6 (0.23)	0	21055	8 (0.04)	0	25	9 (36.00)	0
	2295	2 (0.09)	0	20940	19 (0.09)	0	27	15 (55.56)	0
	3158	8 (0.25)	1	22348	11 (0.05)	0	22	13 (59.09)	0
	981	4 (0.41)	1	13649	1 (0.01)	0	6	3 (50.00)	0
	2258	8 (0.35)	6	23521	7 (0.03)	2	42	26 (61.90)	1
	1279	3 (0.23)	0	11496	2 (0.02)	0	5	5 (100.00)	0
	2141	10 (0.47)	4	19853	20 (0.10)	0	28	22 (78.57)	0
	2450	8 (0.33)	2	25590	12 (0.05)	0	24	14 (58.33)	0
	1260	3 (0.24)	0	11142	10 (0.09)	0	12	8 (66.67)	0
	1597	4 (0.25)	1	19079	5 (0.03)	0	8	1 (12.50)	0
Wales									
	1457	4 (0.27)	0	8688	5 (0.06)	0	16	3 (18.75)	0
	1457	4 (0.27)	0	8688	5 (0.06)	0	16	3 (18.75)	0
Northern Ireland									
	605	2 (0.33)	0	5410	2 (0.04)	0	13	5 (38.46)	0
	605	2 (0.33)	0	5410	2 (0.04)	0	13	5 (38.46)	0
Channel Isles & Isle of Man									
	49	1 (2.04)	0	659	1 (0.15)	0	0	0 (-)	0
	17	0 (0.00)	0	212	0 (0.00)	0	0	0 (-)	0
	20	1 (5.00)	0	207	0 (0.00)	0	0	0 (-)	0
	12	0 (0.00)	0	240	1 (0.42)	0	0	0 (-)	0
Republic of Ireland									
	1406	3 (0.21)	1	10367	5 (0.05)	0	1	0 (0.00)	0
	308	0 (0.00)	0	2932	1 (0.03)	0	0	0 (-)	0
	1098	3 (0.27)	1	7435	4 (0.05)	0	1	0 (0.00)	0
Total	23558	66 (0.28)	16	213797	108 (0.05)	2	229	124 (54.15)	1
Frequency of confirmed positive		1 in 1472							

1. Donors being monitored because of previously reactive, but not confirmed positive, donations.

2. More information about confirmed positive infections in blood donors will be reported in a quarterly surveillance report.

3. Guernsey and Jersey blood centres collect samples for testing, but do not collect donations, from "new donors".

#. One additional HCV infection was detected by NAT testing. This donation was anti-HCV negative and does not appear in tables 1a,b+c.

HIV

Table 2a: HIV infection in blood donor : donor type specific infection rates by centre

Donations collected in September 1999

Blood centre	Donations (cf. table 1a September 1999 report)						Donors being monitored [1]			
	from New Donors[3]			from Known Donors						
	Number tested	Number repeatedly reactive (%)	Number confirmed positive	Number tested	Number repeatedly reactive (%)	Number confirmed positive	Number tested	Number repeatedly reactive (%)	Number confirmed positive	
England										
	20041	29 (0.14)	0	188695	109 (0.06)	0	177	88 (49.72)	0	
	2622	6 (0.23)	0	21063	7 (0.03)	0	17	7 (41.18)	0	
	2295	2 (0.09)	0	20940	9 (0.04)	0	27	4 (14.81)	0	
	3158	4 (0.13)	0	22351	13 (0.06)	0	19	10 (52.63)	0	
	981	1 (0.10)	0	13649	3 (0.02)	0	6	1 (16.67)	0	
	2258	2 (0.09)	0	23529	4 (0.02)	0	34	24 (70.59)	0	
	1279	2 (0.16)	0	11486	12 (0.10)	0	15	15 (100.00)	0	
	2141	2 (0.09)	0	19868	28 (0.14)	0	13	2 (15.38)	0	
	2450	6 (0.24)	0	25586	24 (0.09)	0	28	10 (35.71)	0	
	1260	0 (0.00)	0	11149	4 (0.04)	0	5	4 (80.00)	0	
	1597	4 (0.25)	0	19074	5 (0.03)	0	13	11 (84.62)	0	
Wales										
	1457	0 (0.00)	0	8687	8 (0.09)	0	17	8 (47.06)	0	
	1457	0 (0.00)	0	8687	8 (0.09)	0	17	8 (47.06)	0	
Northern Ireland										
	605	2 (0.33)	0	5421	1 (0.02)	0	2	1 (50.00)	0	
	605	2 (0.33)	0	5421	1 (0.02)	0	2	1 (50.00)	0	
Channel Isles & Isle of Man										
	49	0 (0.00)	0	659	2 (0.30)	0	0	0 (-)	0	
	17	0 (0.00)	0	212	1 (0.47)	0	0	0 (-)	0	
	20	0 (0.00)	0	207	0 (0.00)	0	0	0 (-)	0	
	12	0 (0.00)	0	240	1 (0.42)	0	0	0 (-)	0	
Republic of Ireland										
	1406	3 (0.21)	0	10367	2 (0.02)	0	1	0 (0.00)	0	
	308	0 (0.00)	0	2932	0 (0.00)	0	0	0 (-)	0	
	1098	3 (0.27)	0	7435	2 (0.03)	0	1	0 (0.00)	0	
Total	23558	34 (0.14)	0	213829	122 (0.06)	0	197	97 (49.24)	0	

1. Donors being monitored because of previously reactive, but not confirmed positive, donations.
2. More information about confirmed positive infections will be reported in a quarterly surveillance report.
3. Guerney and Jersey blood centres collect samples for testing, but do not collect donations, from "new donors".

T. PALLIDUM

Table 2a: *T.pallidum* infection in blood donor : donor type specific infection rates by centre

Donations collected in September 1999

Blood centre	Donations (cf. table 1a September 1999 report)								Donors being monitored [1]			
	from New Donors[3]				from Known Donors							
	Number tested	Number repeatedly reactive (%)		Number confirmed positive[2]	Number tested	Number repeatedly reactive (%)		Number confirmed positive[2]	Number tested	Number repeatedly reactive (%)		Number confirmed positive
England												
	20041	12	(0.06)	4	188778	55	(0.03)	2	94	16	(17.02)	0
	2622	0	(0.00)	0	21076	5	(0.02)	0	4	1	(25.00)	0
	2295	1	(0.04)	0	20955	5	(0.02)	0	12	1	(8.33)	0
	3158	3	(0.09)	1	22353	5	(0.02)	0	17	0	(0.00)	0
	981	2	(0.20)	0	13647	14	(0.10)	0	8	3	(37.50)	0
	2258	0	(0.00)	0	23552	8	(0.03)	1	11	4	(36.36)	0
	1279	0	(0.00)	0	11501	4	(0.03)	0	0	0	(-)	0
	2141	1	(0.05)	1	19867	4	(0.02)	0	14	1	(7.14)	0
	2450	2	(0.08)	0	25593	7	(0.03)	0	21	3	(14.29)	0
	1260	2	(0.16)	2	11150	0	(0.00)	0	4	1	(25.00)	0
	1597	1	(0.06)	0	19084	3	(0.02)	1	3	2	(66.67)	0
Wales												
	1457	5	(0.34)	0	8699	3	(0.03)	0	5	0	(0.00)	0
	1457	5	(0.34)	0	8699	3	(0.03)	0	5	0	(0.00)	0
Northern Ireland												
	605	1	(0.17)	0	5419	0	(0.00)	0	4	3	(75.00)	0
	605	1	(0.17)	0	5419	0	(0.00)	0	4	3	(75.00)	0
Channel Isles & Isle of Man												
	49	0	(0.00)	0	659	0	(0.00)	0	0	0	(-)	0
	17	0	(0.00)	0	212	0	(0.00)	0	0	0	(-)	0
	20	0	(0.00)	0	207	0	(0.00)	0	0	0	(-)	0
	12	0	(0.00)	0	240	0	(0.00)	0	0	0	(-)	0
Republic of Ireland												
	1406	0	(0.00)	0	10368	3	(0.03)	1	0	0	(-)	0
	308	0	(0.00)	0	2932	1	(0.03)	0	0	0	(-)	0
	1098	0	(0.00)	0	7436	2	(0.03)	1	0	0	(-)	0
Total	23558	18	(0.08)	4	213923	61	(0.03)	3	103	19	(18.45)	0

1. Donors being monitored because of previously reactive, but not confirmed positive, donations.
2. More information about confirmed positive infections will be reported in a quarterly surveillance report.
3. Guerney and Jersey blood centres collect samples for testing, but do not collect donations, from "new donors".

HEPATITIS B

Table 1b: HBsAg testing of blood donation [1]: cumulative test kit and test kit batch specific results

Donations (collected between 1/10/95 and 30/09/99) tested by test kit batches in use at one or more blood centre during September 1999

Test kit	Batch	Blood Centre [2]	Number [3] Tested	Number reactive (%) Initially		Repeatedly		Confirmatory test results [4] Positive	Negative	Undet.	Pending
			607	1	(0.16)	0	(0.00)	0	0	0	0
			607	1	(0.16)	0	(0.00)	0	0	0	0
			27759	141	(0.51)	18	(0.06)	0	17	1	0
			25046	141	(0.56)	18	(0.07)	0	17	1	0
			2713	0	(0.00)	0	(0.00)	0	0	0	0
			262443	74	(0.03)	30	(0.01)	10	20	0	0
			48051	14	(0.03)	12	(0.02)	3	9	0	0
			3102	4	(0.13)	1	(0.03)	1	0	0	0
			35852	7	(0.02)	5	(0.01)	2	3	0	0
			82244	29	(0.04)	7	(0.01)	3	4	0	0
			3497	1	(0.03)	0	(0.00)	0	0	0	0
			21830	3	(0.01)	1	(0.00)	0	1	0	0
			27894	7	(0.03)	0	(0.00)	0	0	0	0
			6830	1	(0.01)	0	(0.00)	0	0	0	0
			28223	7	(0.02)	4	(0.01)	1	3	0	0
			4920	1	(0.02)	0	(0.00)	0	0	0	0
			518382	2482	(0.48)	439	(0.08)	15	429	4	0
			19115	13	(0.07)	7	(0.04)	0	7	0	0
			43916	208	(0.47)	36	(0.08)	0	36	0	0
			48664	171	(0.35)	26	(0.05)	1	26	1	0
			62861	239	(0.38)	59	(0.09)	0	59	0	0
			20524	53	(0.26)	9	(0.04)	2	9	0	0
			11127	37	(0.33)	10	(0.09)	0	10	0	0
			59925	285	(0.48)	59	(0.10)	4	55	0	0
			22705	86	(0.38)	17	(0.07)	0	21	0	0
			59604	196	(0.33)	38	(0.06)	3	33	1	0
			44109	148	(0.34)	23	(0.05)	0	23	0	0
			47524	486	(1.02)	73	(0.15)	1	73	1	0
			26365	230	(0.87)	21	(0.08)	0	21	0	0
			7594	65	(0.86)	6	(0.08)	1	5	0	0
			7766	35	(0.45)	8	(0.10)	1	7	0	0
			15575	74	(0.48)	19	(0.12)	1	18	0	0
			13439	125	(0.93)	17	(0.13)	1	15	1	0
			7569	31	(0.41)	11	(0.15)	0	11	0	0
			352	0	(0.00)	0	(0.00)	0	0	0	0
			352	0	(0.00)	0	(0.00)	0	0	0	0
			130996	595	(0.45)	204	(0.16)	3	200	1	0
			28068	93	(0.33)	32	(0.11)	2	29	1	0
			60720	215	(0.35)	66	(0.11)	0	66	0	0
			20996	222	(1.06)	81	(0.39)	0	81	0	0
			10542	37	(0.35)	16	(0.15)	0	16	0	0
			10670	28	(0.26)	9	(0.08)	1	8	0	0
			500	1	(0.20)	1	(0.20)	0	1	0	0
			185	1	(0.54)	1	(0.54)	0	1	0	0
			315	0	(0.00)	0	(0.00)	0	0	0	0
Total			**941039**	**3294**	**(0.35)**	**692**	**(0.07)**	**28**	**667**	**6**	**0**

1. Excluding donations from donors being monitored because of previously reactive, but not confirmed to be positive, donations. Details of test results for these donors will be given in the appropriatly dated table 2a (third column).

2. Blood centre(s) at which the test kit batch was in use during the last month are marked with a plus sign (+).

3. Note that the number of test results that are excluded from tables 1a and 1b because they are on donations collected from donors being monitored for previous reactivity to the screening tests is different for each infection. Minor discrepancies between the number of donations tested (by test kit batch) in Tables 1a/b and the number of donations tested (by new and known donor type) in Table 2a may arise for several centres which obtain the denominator counts for these tables from different sources.

4. Discrepancy between the number of donations found to be repeatedly reactive and the sum of the positive, negative, undetermined and pending confirmatory results may arise due to referral for confirmatory testing of donations with screening results in the "grey zone".

HEPATITIS C

Table 1b: Anti-HCV testing of blood donations[1] : cumulative test kit and test kit batch specific results

Donations (collected between 1/10/95 and 30/09/99) tested by test kit batches in use at one or more blood centre during September 1999

Test kit	Batch	Blood centre [2]	Number[3] Tested	Number reactive (%) Initially		Repeatedly		Confirmatory test results [4] Positive	Negative	Undet.	Pending
			22389	24	(0.11)	17	(0.08)	0	11	7	0
			2708	2	(0.07)	1	(0.04)	0	1	0	0
			588	1	(0.17)	0	(0.00)	0	1	0	0
			19093	21	(0.11)	16	(0.08)	0	9	7	0
			66602	49	(0.07)	39	(0.06)	12	21	6	0
			1411	1	(0.07)	1	(0.07)	0	0	1	0
			15123	10	(0.07)	8	(0.05)	1	6	1	0
			28181	24	(0.09)	17	(0.06)	10	7	0	0
			3590	2	(0.06)	2	(0.06)	1	0	1	0
			4912	1	(0.02)	1	(0.02)	0	0	1	0
			3240	1	(0.03)	1	(0.03)	0	1	0	0
			4223	8	(0.19)	7	(0.17)	0	5	2	0
			5922	2	(0.03)	2	(0.03)	0	2	0	0
			240	1	(0.42)	1	(0.42)	0	1	0	0
			240	1	(0.42)	1	(0.42)	0	1	0	0
			151846	80	(0.05)	55	(0.04)	4	48	3	0
			22500	9	(0.04)	7	(0.03)	0	7	0	0
			5603	1	(0.02)	0	(0.00)	0	0	0	0
			683	1	(0.15)	1	(0.15)	0	1	0	0
			13268	6	(0.05)	5	(0.04)	1	3	1	0
			23406	18	(0.08)	12	(0.05)	0	12	0	0
			7695	3	(0.04)	0	(0.00)	0	0	0	0
			81	0	(0.00)	0	(0.00)	0	0	0	0
			23386	7	(0.03)	6	(0.03)	1	5	0	0
			21105	10	(0.05)	8	(0.04)	0	8	0	0
			3776	5	(0.13)	2	(0.05)	0	2	0	0
			23146	14	(0.06)	10	(0.04)	1	8	1	0
			7197	6	(0.08)	4	(0.06)	1	2	1	0
			259006	549	(0.21)	235	(0.09)	15	167	52	1
			52466	191	(0.36)	60	(0.11)	2	54	4	0
			29260	84	(0.29)	46	(0.16)	5	36	5	0
			41003	87	(0.21)	31	(0.08)	4	26	1	0
			57949	93	(0.16)	34	(0.06)	3	23	8	0
			44858	52	(0.12)	37	(0.08)	1	4	31	1
			33470	42	(0.13)	27	(0.08)	0	24	3	0
Total			**500083**	**703**	**(0.14)**	**347**	**(0.07)**	**31**	**248**	**68**	**1**

1. Excluding donations from donors being monitored because of previously reactive, but not confirmed to be positive, donations. Details of test results for these donors will be given in the appropriatly dated table 2a (third column).

2. Blood centre(s) at which the test kit batch was in use during the last month are marker with a plus sign (+).

3. Note that the number of test results that are excluded from tables 1a and 1b because they are on donations collected from donors being monitored for previous reactivity to the screening tests is different for each infection. Minor discrepancies between the number of donations tested (by test kit batch) in Tables 1a/b and the number of donations tested (by new and known donor type) in Table 2a may arise for several centres which obtain the denominator counts for these tables from different sources.

4. Discrepancy between the number of donations found to be repeatedly reactive and the sum of the positive, negative, undetermined and pending confirmatory results may arise due to referral for confirmatory testing of donations with screening results in the "grey zone".

HIV

Table 1b: Anti-HIV testing of blood donations[1] : cumulative test kit and test kit batch specific results

Donations (collected between 1/10/95 and 30/09/99) tested by test kit batches in use at one or more blood centre during September 1999

Test kit	Batch	Blood Centre [2]	Number[3] Tested	Number reactive (%) Initially		Repeatedly		Confirmatory test results [4] Positive	Negative	Undet.	Pending
			7681	4	(0.05)	3	(0.04)	0	3	0	0
			7681	4	(0.05)	3	(0.04)	0	3	0	0
			439	1	(0.23)	1	(0.23)	0	1	0	0
			439	1	(0.23)	1	(0.23)	0	1	0	0
			144762	169	(0.12)	68	(0.05)	1	61	6	0
			28200	27	(0.10)	9	(0.03)	0	9	0	0
			38695	48	(0.12)	28	(0.07)	0	22	6	0
			3643	6	(0.16)	2	(0.05)	0	2	0	0
			33290	41	(0.12)	14	(0.04)	0	14	0	0
			27873	40	(0.14)	13	(0.05)	1	12	0	0
			6830	2	(0.03)	1	(0.01)	0	1	0	0
			4909	5	(0.10)	1	(0.02)	0	1	0	0
			1322	0	(0.00)	0	(0.00)	0	0	0	0
			19445	57	(0.29)	30	(0.15)	0	30	0	0
			7521	21	(0.28)	20	(0.27)	0	20	0	0
			11924	36	(0.30)	10	(0.08)	0	10	0	0
			232375	300	(0.13)	173	(0.07)	4	167	3	0
			8086	6	(0.07)	3	(0.04)	0	3	0	0
			18080	42	(0.23)	13	(0.07)	1	12	0	0
			54426	59	(0.11)	37	(0.07)	1	34	2	0
			40043	52	(0.13)	38	(0.09)	1	37	0	0
			61082	77	(0.13)	44	(0.07)	1	43	1	0
			7300	7	(0.10)	1	(0.01)	0	1	0	0
			4737	2	(0.04)	2	(0.04)	0	2	0	0
			22238	32	(0.14)	19	(0.09)	0	19	0	0
			396	1	(0.25)	1	(0.25)	0	1	0	0
			9215	10	(0.11)	9	(0.10)	0	9	0	0
			6772	12	(0.18)	6	(0.09)	0	6	0	0
			344895	284	(0.08)	168	(0.05)	2	165	1	0
			58723	42	(0.07)	19	(0.03)	1	17	1	0
			48785	20	(0.04)	9	(0.02)	1	8	0	0
			22054	42	(0.19)	20	(0.09)	0	20	0	0
			10801	6	(0.06)	4	(0.04)	0	4	0	0
			19811	11	(0.06)	7	(0.04)	0	6	0	0
			20485	15	(0.07)	12	(0.06)	0	12	0	0
			28115	18	(0.06)	12	(0.04)	0	12	0	0
			30222	35	(0.12)	10	(0.03)	0	10	0	0
			21427	29	(0.14)	26	(0.12)	0	26	0	0
			8925	5	(0.06)	4	(0.04)	0	4	0	0
			41691	33	(0.08)	25	(0.06)	0	25	0	0
			12413	9	(0.07)	6	(0.05)	0	7	0	0
			4370	2	(0.05)	2	(0.05)	0	2	0	0
			994	0	(0.00)	0	(0.00)	0	0	0	0
			10054	10	(0.10)	10	(0.10)	0	10	0	0
			3920	7	(0.18)	2	(0.05)	0	2	0	0
			2105	0	(0.00)	0	(0.00)	0	0	0	0
			444	2	(0.45)	1	(0.23)	0	1	0	1
			240	0	(0.00)	0	(0.00)	0	0	0	0
			158	2	(1.27)	1	(0.63)	0	1	0	1
			46	0	(0.00)	0	(0.00)	0	0	0	0
Total			**750041**	**817**	**(0.11)**	**444**	**(0.06)**	**7**	**428**	**10**	**1**

1. Excluding donations from donors being monitored because of previously reactive, but not confirmed to be positive, donations. Details of test results for these donors will be given in the appropriatly dated Table 2a (third column).

2. Blood centre(s) at which the test kit batch was in use during the last month are marked with a plus sign (+).

3. Note that the number of test results that are excluded from tables 1a and 1b because they are on donations collected from donors being monitored for previous reactivity to the screening tests is different for each infection. Minor discrepancies between the number of donations tested (by test kit batch) in Tables 1a/b and the number of donations tested (by new and known donor type) in Table 2a may arise for several centres which obtain the denominator counts for these tables from different sources.

4. Discrepancy between the number of donations found to be repeatedly reactive and the sum of the positive, negative, undetermined and pending confirmatory results may arise due to referral for confirmatory testing of donations with screening results in the "grey zone".

T. PALLIDUM

Table 1b: *T.pallidum* testing of blood donation [1] : cumulative test kit and test kit batch specific result

Donations (collected between 1/10/95 and 30/09/99) tested by test k batches in use at one or more blood centre during September 19

Test kit	Batch	Blood centre [2]	Number [3] Tested	Number reactive (%) Initially		Repeatedly		Confirmatory test results [4] Positive	Negative	Undet.	Penc
			492	0	(0.00)	0	(0.00)	0	0	0	
			492	0	(0.00)	0	(0.00)	0	0	0	
			28683	225	(0.78)	50	(0.17)	0	50	0	
			28683	225	(0.78)	50	(0.17)	0	50	0	
			1233	0	(0.00)	0	(0.00)	0	0	0	
			1233	0	(0.00)	0	(0.00)	0	0	0	
			547887	650	(0.12)	155	(0.03)	17	127	10	
			1011	2	(0.20)	0	(0.00)	0	0	0	
			959	4	(0.42)	3	(0.31)	0	3	0	
			30317	17	(0.06)	4	(0.01)	0	3	1	
			21741	18	(0.08)	3	(0.01)	0	3	0	
			24987	21	(0.08)	10	(0.04)	1	8	1	
			3497	5	(0.14)	4	(0.11)	0	3	1	
			22113	33	(0.15)	4	(0.02)	1	3	0	
			19171	49	(0.26)	7	(0.04)	1	6	0	
			23536	28	(0.12)	9	(0.04)	2	7	0	
			22741	3	(0.01)	1	(0.00)	1	0	0	
			20047	21	(0.10)	10	(0.05)	4	6	0	
			16171	16	(0.10)	5	(0.03)	0	4	1	
			8926	4	(0.04)	2	(0.02)	2	0	0	
			24076	20	(0.08)	7	(0.03)	0	6	0	
			220	0	(0.00)	0	(0.00)	0	0	0	
			10691	8	(0.07)	3	(0.03)	0	3	0	
			18829	11	(0.06)	1	(0.01)	0	1	0	
			3590	4	(0.11)	1	(0.03)	0	1	0	
			19363	57	(0.29)	7	(0.04)	0	8	0	
			44901	34	(0.08)	12	(0.03)	0	11	1	
			16418	5	(0.03)	4	(0.02)	1	3	0	
			20250	18	(0.09)	3	(0.01)	0	3	0	
			27182	25	(0.09)	6	(0.02)	0	6	0	
			3240	4	(0.12)	1	(0.03)	0	1	0	
			5982	8	(0.13)	5	(0.08)	0	5	0	
			4293	27	(0.63)	1	(0.02)	0	1	0	
			23162	11	(0.05)	3	(0.01)	1	1	1	
			27436	36	(0.13)	7	(0.03)	0	7	0	
			25511	32	(0.13)	8	(0.03)	1	4	2	
			3487	13	(0.37)	2	(0.06)	1	1	0	
			26609	97	(0.36)	15	(0.06)	1	14	0	
			21021	15	(0.07)	5	(0.02)	0	3	2	
			4304	4	(0.09)	2	(0.05)	0	2	0	
			2105	0	(0.00)	0	(0.00)	0	0	0	
			52521	43	(0.08)	15	(0.03)	1	13	1	
			52521	43	(0.08)	15	(0.03)	1	13	1	
			68502	79	(0.12)	33	(0.05)	1	30	3	
			24823	58	(0.23)	25	(0.10)	1	21	3	
			41640	18	(0.04)	7	(0.02)	0	7	0	
			2039	3	(0.15)	1	(0.05)	0	2	0	
			13298	24	(0.18)	3	(0.02)	0	3	0	
			8108	14	(0.17)	2	(0.02)	0	2	0	
			5190	10	(0.19)	1	(0.02)	0	1	0	
Total			712616	1021	(0.14)	256	(0.04)	19	223	14	

1. Excluding donations from donors being monitored because of previously reactive, but not confirmed to be positive, donations. Details test results for these donors will be given in the appropriately dated table 2a (third column).

2. Blood centre(s) at which the test kit batch was in use during the last month are marked with a plus sign (+).

3. Note that the number of test results that are excluded from tables 1a and 1b because they are on donations collected from donors bein monitored for previous reactivity to the screening tests is different for each infection. Minor discrepancies between the number of donations tested (by test kit batch) in Tables 1a/b and the number of donations tested (by new and known donor type) in Table 2a may arise for several centres which obtain the denominator counts for these tables from different sources.

4. Discrepancy between the number of donations found to be repeatedly reactive and the sum of the positive, negative, undetermined anc pending confirmatory results may arise due to referral for confirmatory testing of donations with screening results in the "grey zone".

HEPATITIS B

Table 1c: HBsAg positivity in blood donor : donation type specific repeatedly reactive rates by test kit

Donations collected during the 12 months prior to 30/09/99 (excluding donations tested by blood centres during a month in which more than one test kit was used by the blood centre)

Blood centre	Donations from New Donors				Donations from Known Donors				Donors being monitored [1]			
	Number tested	Number repeatedly reactive	(%)	Number confirmed positive	Number tested	Number repeatedly reactive	(%)	Number confirmed positive	Number tested	Number repeatedly reactive	(%)	Number confirmed positive
	33	0	(0.00)	0	780	0	(0.00)	0	5	1	(20.00)	0
	33	0	(0.00)	0	780	0	(0.00)	0	5	1	(20.00)	0
	179	0	(0.00)	0	2506	0	(0.00)	0	1	0	(0.00)	0
	179	0	(0.00)	0	2506	0	(0.00)	0	1	0	(0.00)	0
	25499	12	(0.05)	1	110684	76	(0.07)	0	62	23	(37.10)	0
	18710	10	(0.05)	1	55164	68	(0.12)	0	45	14	(31.11)	0
	6789	2	(0.03)	0	55520	8	(0.01)	0	17	9	(52.94)	0
	54674	26	(0.05)	17	413564	46	(0.01)	2	89	15	(16.85)	0
	5352	0	(0.00)	0	36566	4	(0.01)	1	1	1	(100.00)	0
	13181	5	(0.04)	4	99199	6	(0.01)	0	0	0	(-)	0
	36141	21	(0.06)	13	277799	36	(0.01)	1	88	14	(15.91)	0
	60	0	(0.00)	0	1063	1	(0.09)	0	0	0	(-)	0
	60	0	(0.00)	0	1063	1	(0.09)	0	0	0	(-)	0
	177254	304	(0.17)	62	1365692	1522	(0.11)	8	2061	361	(17.52)	2
	33721	30	(0.09)	8	239456	154	(0.06)	4	264	35	(13.26)	0
	28972	34	(0.12)	7	255395	303	(0.12)	0	351	97	(27.64)	0
	37178	71	(0.19)	9	254853	266	(0.10)	0	357	50	(14.01)	2
	24575	53	(0.22)	18	217803	190	(0.09)	2	304	75	(24.67)	0
	34667	83	(0.24)	14	271290	502	(0.19)	1	664	88	(13.25)	0
	18141	33	(0.18)	6	126895	107	(0.08)	1	121	16	(13.22)	0
	123	0	(0.00)	0	2917	0	(0.00)	0	0	0	(-)	0
	123	0	(0.00)	0	2917	0	(0.00)	0	0	0	(-)	0
	50868	104	(0.20)	8	462335	541	(0.12)	2	540	243	(45.00)	0
	16112	36	(0.22)	4	146674	120	(0.08)	0	140	68	(48.57)	0
	11043	16	(0.14)	0	90748	154	(0.17)	2	14	14	(100.00)	0
	23713	52	(0.22)	4	224913	267	(0.12)	0	386	161	(41.71)	0
	30	0	(0.00)	0	843	1	(0.12)	0	0	0	(-)	0
	30	0	(0.00)	0	843	1	(0.12)	0	0	0	(-)	0
Total	308720	446	(0.14)	88	2360384	2187	(0.09)	12	2758	643	(23.31)	2

1. Donors being monitored because of previously reactive, but not confirmed positive, donations.

HEPATITIS C

Table 1c: Anti-HCV positivity in blood donor : donation type specific repeatedly reactive rates by test kit
Donations collected during the 12 months prior to 30/09/99 (excluding donations tested by blood centres during a month in which more than one test kit was used by the blood centre)

Blood centre	Donations								Donors being monitored[1]			
	from New Donors				from Known Donors							
	Number tested	Number repeatedly reactive	(%)	Number confirmed positive	Number tested	Number repeatedly reactive	(%)	Number confirmed positive	Number tested	Number repeatedly reactive	(%)	Number confirmed positive
	25589	46	(0.18)	1	112139	132	(0.12)	2	513	220	(42.88)	2
	18710	32	(0.17)	1	54851	49	(0.09)	0	358	163	(45.53)	0
	90	0	(0.00)	0	1904	1	(0.05)	0	2	1	(50.00)	0
	6789	14	(0.21)	0	55384	82	(0.15)	2	153	56	(36.60)	2
	70307	182	(0.26)	28	510328	388	(0.08)	16	1673	655	(39.15)	8
	15633	46	(0.29)	11	98106	121	(0.12)	3	242	80	(33.06)	0
	5352	12	(0.22)	1	36567	28	(0.08)	1	0	0	(-)	0
	13181	27	(0.20)	2	99188	59	(0.06)	1	11	0	(0.00)	0
	36141	97	(0.27)	14	276467	180	(0.07)	11	1420	575	(40.49)	8
	202	1	(0.50)	0	3014	6	(0.20)	0	8	6	(75.00)	0
	202	1	(0.50)	0	3014	6	(0.20)	0	8	6	(75.00)	0
	50991	83	(0.16)	23	465195	114	(0.02)	1	597	145	(24.29)	1
	123	2	(1.63)	1	2913	0	(0.00)	0	4	3	(75.00)	0
	16112	26	(0.16)	11	146736	30	(0.02)	0	78	25	(32.05)	0
	11043	16	(0.14)	1	90734	42	(0.05)	1	28	11	(39.29)	0
	23713	39	(0.16)	10	224812	42	(0.02)	0	487	106	(21.77)	1
	177254	363	(0.20)	89	1365512	901	(0.07)	14	2241	779	(34.76)	1
	33721	61	(0.18)	11	239405	178	(0.07)	1	315	91	(28.89)	0
	28972	56	(0.19)	14	255446	173	(0.07)	4	300	114	(38.00)	0
	37178	59	(0.16)	14	254936	115	(0.05)	2	274	67	(24.45)	1
	24575	94	(0.38)	20	217605	191	(0.09)	4	502	234	(46.61)	0
	34667	67	(0.19)	20	271283	135	(0.05)	3	671	245	(36.51)	0
	18141	26	(0.14)	10	126837	109	(0.09)	0	179	28	(15.64)	0
Total	324343	675	(0.21)	141	2456188	1541	(0.06)	33	5032	1805	(35.87)	12

1. Donors being monitored because of previously reactive, but not confirmed positive, donations.

HIV

Table 1c: Anti-HIV positivity in blood donor : donation type specific repeatedly reactive rates by test kit
Donations collected during the 12 months prior to 30/09/99 (excluding donations tested by blood centres during a month in which more than one test kit was used by the blood centre)

Blood centre	Donations from New Donors				Donations from Known Donors				Donors being monitored[1]			
	Number tested	Number repeatedly reactive	(%)	Number confirmed positive	Number tested	Number repeatedly reactive	(%)	Number confirmed positive	Number tested	Number repeatedly reactive	(%)	Number confirmed positive
	5762	0	(0.00)	0	668	1	(0.15)	0	12	4	(33.33)	0
	5762	0	(0.00)	0	668	1	(0.15)	0	12	4	(33.33)	0
	19737	22	(0.11)	0	109926	34	(0.03)	0	140	54	(38.57)	0
	12948	17	(0.13)	0	54417	11	(0.02)	0	112	43	(38.39)	0
	6789	5	(0.07)	0	55509	23	(0.04)	0	28	11	(39.29)	0
	202	0	(0.00)	0	3022	1	(0.03)	0	0	0	(-)	0
	202	0	(0.00)	0	3022	1	(0.03)	0	0	0	(-)	0
	70307	91	(0.13)	2	511227	237	(0.05)	4	774	318	(41.09)	0
	15633	25	(0.16)	0	98192	66	(0.07)	0	156	49	(31.41)	0
	5352	4	(0.07)	0	36566	15	(0.04)	1	1	1	(100.00)	0
	13181	20	(0.15)	1	99198	42	(0.04)	0	1	0	(0.00)	0
	36141	42	(0.12)	1	277271	114	(0.04)	3	616	268	(43.51)	0
	71	1	(1.41)	0	1195	2	(0.17)	0	0	0	(-)	0
	71	1	(1.41)	0	1195	2	(0.17)	0	0	0	(-)	0
	88337	129	(0.15)	7	747324	624	(0.08)	7	1400	488	(34.86)	0
	28972	35	(0.12)	1	255295	209	(0.08)	3	451	157	(34.81)	0
	123	0	(0.00)	0	2917	4	(0.14)	0	0	0	(-)	0
	24575	41	(0.17)	3	217827	174	(0.08)	2	280	72	(25.71)	0
	34667	53	(0.15)	3	271285	237	(0.09)	2	669	259	(38.71)	0
	2114	0	(0.00)	1	17056	0	(0.00)	0	7	0	(0.00)	0
	2114	0	(0.00)	1	17056	0	(0.00)	0	7	0	(0.00)	0
	139908	155	(0.11)	3	1083745	555	(0.05)	3	1076	318	(29.55)	0
	33721	36	(0.11)	2	239483	83	(0.03)	2	237	70	(29.54)	0
	37178	32	(0.09)	1	254996	97	(0.04)	0	214	57	(26.64)	0
	16112	25	(0.16)	0	146588	88	(0.06)	1	226	49	(21.68)	0
	11043	12	(0.11)	0	90735	103	(0.11)	0	27	16	(59.26)	0
	18141	18	(0.10)	0	126864	70	(0.06)	0	152	32	(21.05)	0
	23713	32	(0.13)	0	225079	114	(0.05)	0	220	94	(42.73)	0
	19	2	(10.53)	0	705	1	(0.14)	0	6	3	(50.00)	0
	19	2	(10.53)	0	705	1	(0.14)	0	6	3	(50.00)	0
Total	326457	400	(0.12)	13	2474868	1455	(0.06)	14	3415	1185	(34.70)	0

1. Donors being monitored because of previously reactive, but not confirmed positive, donations.

T. PALLIDUM

Table 1c: *T.pallidum* antibody positivity in donors donation type specific repeatedly reactive rates by test kit

Donations collected during the 12 months prior to 30/09/99 (excluding donations tested by blood centres during a month in which more than one test kit was used by the blood centre)

Blood centre	Donations from New Donors				Donations from Known Donors				Donors being monitored [1]			
	Number tested	Number repeatedly reactive	(%)	Number confirmed positive	Number tested	Number repeatedly reactive	(%)	Number confirmed positive	Number tested	Number repeatedly reactive	(%)	Number confirmed positive
BECTON DICKINSON RPR	467	1	(0.21)	0	5322	0	(0.00)	0	0	0	(-)	0
	377	0	(0.00)	0	3416	0	(0.00)	0	0	0	(-)	0
	90	1	(1.11)	0	1906	0	(0.00)	0	0	0	(-)	0
CENTOCOR	16112	12	(0.07)	0	146571	86	(0.06)	0	243	42	(17.28)	0
	16112	12	(0.07)	0	146571	86	(0.06)	0	243	42	(17.28)	0
IMMUTREP RPR	2457	1	(0.04)	0	14821	0	(0.00)	0	0	0	(-)	0
	2457	1	(0.04)	0	14821	0	(0.00)	0	0	0	(-)	0
MUREX TPHA VD35	214721	171	(0.08)	35	1692514	872	(0.05)	31	1719	269	(15.65)	3
	33721	12	(0.04)	3	239636	32	(0.01)	4	84	15	(17.86)	0
	28972	26	(0.09)	2	255393	132	(0.05)	3	353	50	(14.16)	0
	37178	18	(0.05)	4	255114	106	(0.04)	1	96	14	(14.58)	0
	2518	2	(0.08)	0	18330	17	(0.09)	2	0	0	(-)	0
	11236	9	(0.08)	3	82851	51	(0.06)	10	0	0	(-)	0
	24575	38	(0.15)	10	217659	199	(0.09)	1	448	46	(10.27)	0
	34667	47	(0.14)	7	271405	245	(0.09)	5	549	79	(14.39)	0
	18141	5	(0.03)	3	126974	5	(0.00)	0	42	7	(16.67)	1
	23713	14	(0.06)	3	225152	85	(0.04)	5	147	58	(39.46)	2
MUREX VDRL	4451	2	(0.04)	0	32024	6	(0.02)	1	0	0	(-)	0
	4451	2	(0.04)	0	32024	6	(0.02)	1	0	0	(-)	0
NEWMARKET LAB	36141	14	(0.04)	4	277659	75	(0.03)	2	228	64	(28.07)	6
	36141	14	(0.04)	4	277659	75	(0.03)	2	228	64	(28.07)	6
OLYMPUS PK	15824	10	(0.06)	1	135052	42	(0.03)	1	21	19	(90.48)	0
	15824	10	(0.06)	1	135052	42	(0.03)	1	21	19	(90.48)	0
RANDOX TPHA	18710	2	(0.01)	0	55145	17	(0.03)	0	64	7	(10.94)	1
	18710	2	(0.01)	0	55145	17	(0.03)	0	64	7	(10.94)	1
Total	308883	213	(0.07)	40	2359108	1098	(0.05)	35	2275	401	(17.63)	10

1. Donors being monitored because of previously reactive, but not confirmed positive, donations.

HEPATITIS B

Table 2b: HBV infection in blood donor : cumulative donation type specific infection rates by centre

Donations collected between 1/10/95 and 30/09/99

Blood centre	Donations from New Donors[3]			Donations from Known Donors			Donors being monitored[1]		
	Number tested	Number repeatedly reactive (%)	Number confirmed positive (%)[2]	Number tested	Number repeatedly reactive (%)	Number confirmed positive[2]	Number tested	Number repeatedly reactive (%)	Number confirmed positive
England	109390	1482 (0.13)	378 (0.03)	8868582	5018 (0.06)	57	5941	1697 (28.56)	9
	4878	4 (0.08)	1	1487	2 (0.13)	2	0	0 (-)	0
	99724	141 (0.14)	27	940579	538 (0.06)	7	873	206 (23.60)	0
	138235	217 (0.16)	40	905062	666 (0.07)	1	911	248 (27.22)	1
	117663	179 (0.15)	26	916943	602 (0.07)	0	671	100 (14.90)	2
	13941	12 (0.09)	4	111473	22 (0.02)	0	41	11 (26.83)	0
	4432	2 (0.05)	2	26985	7 (0.03)	0	2	1 (50.00)	0
	72083	124 (0.17)	19	608178	363 (0.06)	2	372	147 (39.52)	1
	114873	50 (0.04)	32	908783	115 (0.01)	8	161	35 (21.74)	1
	22367	12 (0.05)	10	236100	23 (0.01)	7	26	8 (30.77)	1
	53325	50 (0.09)	8	642507	280 (0.04)	5	59	59 (100.00)	1
	127917	238 (0.19)	107	856008	416 (0.05)	9	675	143 (21.19)	0
	25850	35 (0.14)	7	170013	107 (0.06)	2	156	46 (29.49)	0
	140599	210 (0.15)	46	1204387	1138 (0.09)	8	1292	361 (27.94)	1
	78336	70 (0.09)	22	450596	168 (0.04)	2	160	37 (23.13)	1
	95167	138 (0.15)	27	889481	571 (0.06)	4	542	295 (54.43)	0
Wales	69635	29 (0.04)	16 (0.02)	396592	80 (0.02)	6	75	11 (14.67)	1
	69635	29 (0.04)	16	396592	80 (0.02)	6	75	11 (14.67)	1
Northern Ireland	51449	18 (0.03)	2 (0.00)	256152	103 (0.04)	0	99	46 (46.46)	0
	51449	18 (0.03)	2	256152	103 (0.04)	0	99	46 (46.46)	0
Channel Isles & Isle of Man	2021	2 (0.10)	0 (0.00)	31075	24 (0.08)	0	20	6 (30.00)	0
	518	2 (0.39)	0	7642	19 (0.25)	0	4	0 (0.00)	0
	531	0 (0.00)	0	10324	1 (0.01)	0	2	2 (100.00)	0
	972	0 (0.00)	0	13109	4 (0.03)	0	14	4 (28.57)	0
Republic of Ireland	72422	36 (0.05)	16 (0.02)	579212	82 (0.01)	4	41	14 (34.15)	1
	20695	6 (0.03)	2	149738	19 (0.01)	1	9	9 (100.00)	1
	51727	30 (0.06)	14	429474	63 (0.01)	3	32	5 (15.63)	0
Total	1304917	1567 (0.12)	412 (0.03)	10131613	5307 (0.05)	67	6176	1774 (28.72)	11
Frequency of confirmed positive		1 in 3,167			1 in 151,218				

1. Donors being monitored because of previously reactive, but not confirmed positive, donations.

2. More information about confirmed positive infections in blood donors will be reported in a quarterly surveillance report.

3. Guerney and Jersey blood centres collect samples for testing, but do not collect donations, from "new donors".

HEPATITIS C

Table 2b: HCV infection in blood donor : cumulative donation type specific infection rates by centre

Donations collected between 1/10/95 and 30/09/99

Blood centre	Donations from New Donors[3]			Donations from Known Donors			Donors being monitored[1]		
	Number tested	Number repeatedly reactive (%)	Number confirmed positive (%)[2]	Number tested	Number repeatedly reactive (%)	Number confirmed positive[2]	Number tested	Number repeatedly reactive (%)	Number confirmed positive[2]
England	1109390	2775 (0.25)	616 (0.06)	8860959	7548 (0.09)	176	13564	6260 (46.15)	52
	4878	2 (0.04)	0	1486	1 (0.07)	0	1	0 (0.00)	0
	99724	190 (0.19)	44	940380	513 (0.05)	17	1072	379 (35.35)	6
	138235	297 (0.21)	58	904456	861 (0.10)	12	1517	551 (36.32)	2
	117663	245 (0.21)	68	916759	516 (0.06)	8	855	266 (31.11)	4
	13941	48 (0.34)	9	111364	106 (0.10)	1	150	73 (48.67)	1
	4432	7 (0.16)	1	26921	25 (0.09)	7	66	53 (80.30)	2
	72083	166 (0.23)	45	608255	154 (0.03)	2	295	135 (45.76)	0
	114873	292 (0.25)	65	906740	952 (0.10)	38	2204	1426 (64.70)	15
	22367	49 (0.22)	17	235637	122 (0.05)	23	489	283 (57.87)	5
	53325	175 (0.33)	16	642197	783 (0.12)	10	369	369 (100.00)	2
	127917	538 (0.42)	110	854699	1168 (0.14)	18	1984	972 (48.99)	4
	25850	41 (0.16)	9	169931	175 (0.10)	6	238	62 (26.05)	1
	140599	294 (0.21)	108	1203341	958 (0.08)	28	2338	906 (38.75)	8
	78336	210 (0.27)	25	450272	568 (0.13)	3	484	252 (52.07)	0
	95167	221 (0.23)	41	888521	646 (0.07)	3	1502	533 (35.49)	2
Wales	69635	127 (0.18)	46 (0.07)	396215	384 (0.10)	13	452	217 (48.01)	7
	69635	127 (0.18)	46	396215	384 (0.10)	13	452	217 (48.01)	7
Northern Ireland	51449	144 (0.28)	9 (0.02)	255133	289 (0.11)	3	1118	677 (60.55)	0
	51449	144 (0.28)	9	255133	289 (0.11)	3	1118	677 (60.55)	0
Channel Isles & Isle of Man	2021	5 (0.25)	1 (0.05)	31070	28 (0.09)	2	25	20 (80.00)	0
	518	0 (0.00)	0	7644	9 (0.12)	0	2	1 (50.00)	0
	531	3 (0.56)	1	10316	4 (0.04)	1	10	9 (90.00)	0
	972	2 (0.21)	0	13110	15 (0.11)	1	13	10 (76.92)	0
Republic of Ireland	72422	262 (0.36)	23 (0.03)	578402	715 (0.12)	15	851	201 (23.62)	0
	20695	70 (0.34)	6	149657	145 (0.10)	2	90	90 (100.00)	0
	51727	192 (0.37)	17	428745	570 (0.13)	13	761	111 (14.59)	0
Total	1304917	3313 (0.25)	695 (0.00)	10121779	8964 (0.09)	209	16010	7375 (46.06)	59
Frequency of confirmed positive			1 in 1,878			1 in 48,430			

1. Donors being monitored because of previously reactive, but not confirmed positive, donations.
2. More information about confirmed positive infections in blood donors will be reported in a quarterly surveillance report.
3. Guernsey and Jersey blood centres collect samples for testing, but do not collect donations, from "new donors".

#. An additional HCV infection was detected by NAT testing. This donation was anti-HCV negative and does not appear in tables 1a,b+c.

Table 2b: HIV infection in blood donor : cumulative donation type specific infection rates by centre

Donations collected between 1/10/95 and 30/09/99

Blood centre	Donations from New Donors[3]				Donations from Known Donors				Donors being monitored[1]			
	Number tested	Number repeatedly reactive (%)		Number confirmed positive (%)[2]	Number tested	Number repeatedly reactive (%)		Number confirmed positive[2]	Number tested	Number repeatedly reactive (%)		Number confirmed positive[2]
England												
	1109390	1157	(0.10)	55 (0.00)	8868237	4267	(0.05)	38	6286	3027	(48.15)	0
	4878	0	(0.00)	0	1486	1	(0.07)	0	1	1	(100.00)	0
	99724	103	(0.10)	5	940944	388	(0.04)	4	508	231	(45.47)	0
	138235	123	(0.09)	4	905230	468	(0.05)	3	743	300	(40.38)	0
	117663	141	(0.12)	5	917043	438	(0.05)	1	571	183	(32.05)	0
	13941	20	(0.14)	0	111380	64	(0.06)	0	134	85	(63.43)	0
	4432	1	(0.02)	0	26958	15	(0.06)	0	29	18	(62.07)	0
	72083	84	(0.12)	2	608112	415	(0.07)	3	438	123	(28.08)	0
	114873	143	(0.12)	3	907757	549	(0.06)	3	1187	690	(58.13)	0
	22367	19	(0.08)	1	235965	109	(0.05)	2	161	56	(34.78)	0
	53325	79	(0.15)	1	642408	313	(0.05)	3	158	158	(100.00)	0
	127917	119	(0.09)	15	856177	307	(0.04)	7	506	179	(35.38)	0
	25850	15	(0.06)	0	170040	74	(0.04)	0	129	31	(24.03)	0
	140599	138	(0.10)	16	1204643	567	(0.05)	9	1036	556	(53.67)	0
	78336	83	(0.11)	2	450444	241	(0.05)	0	312	181	(58.01)	0
	95167	89	(0.09)	1	889650	318	(0.04)	3	373	235	(63.00)	0
Wales												
	69635	65	(0.09)	1 (0.00)	396369	288	(0.07)	0	298	109	(36.58)	0
	69635	65	(0.09)	1	396369	288	(0.07)	0	298	109	(36.58)	0
Northern Ireland												
	51449	92	(0.18)	0 (0.00)	255810	86	(0.03)	0	441	246	(55.78)	0
	51449	92	(0.18)	0	255810	86	(0.03)	0	441	246	(55.78)	0
Channel Isles & Isle of Man												
	2021	6	(0.30)	0 (0.00)	31077	34	(0.11)	1	18	15	(83.33)	0
	518	4	(0.77)	0	7639	23	(0.30)	0	7	7	(100.00)	0
	531	0	(0.00)	0	10325	8	(0.08)	0	1	1	(100.00)	0
	972	2	(0.21)	0	13113	3	(0.02)	1	10	7	(70.00)	0
Republic of Ireland												
	72422	123	(0.17)	3 (0.00)	578909	336	(0.06)	2	344	50	(14.53)	0
	20695	28	(0.14)	0	149723	74	(0.05)	2	24	24	(100.00)	0
	51727	95	(0.18)	3	429186	262	(0.06)	0	320	26	(8.13)	0
Total	1304917	1443	(0.11)	59 (0.00)	10130402	5011	(0.05)	41	7387	3447	(46.66)	0
Frequency of confirmed positive				1 in 22117				1 in 247,083				

1. Donors being monitored because of previously reactive, but not confirmed positive, donations.
2. More information about confirmed positive infections will be reported in a quarterly surveillance report.
3. Guernsey and Jersey blood centres collect samples for testing, but do not collect donations, from "new donors".

T. PALLIDUM

Table 2b: *T.pallidum* infection in blood donor : cumulative donation type specific infection rates by centre

Donations collected between 1/10/95 and 30/09/99

Blood centre	Donations from New Donors			Donations from Known Donors			Donors being monitored [1]		
	Number tested	Number repeatedly reactive (%)	Number[2] confirmed positive (%)	Number tested	Number repeatedly reactive (%)	Number[2] confirmed positive	Number tested	Number repeatedly reactive (%)	Number[2] confirmed positive
England									
	1109390	891 (0.08)	176 (0.02)	8870055	3484 (0.04)	123	4468	1245 (27.86)	61
	4878	0 (0.00)	0	1484	2 (0.13)	0	3	1 (33.33)	0
	99724	39 (0.04)	7	941170	164 (0.02)	6	282	38 (13.48)	3
	138235	182 (0.13)	26	905033	558 (0.06)	15	940	256 (27.23)	5
	117663	80 (0.07)	19	917218	238 (0.03)	4	396	54 (13.64)	1
	13941	8 (0.06)	1	111475	8 (0.01)	0	39	28 (71.79)	0
	4432	4 (0.09)	2	26963	8 (0.03)	1	24	2 (8.33)	2
	72083	118 (0.16)	4	608074	529 (0.09)	2	476	161 (33.82)	2
	114873	89 (0.08)	14	908262	458 (0.05)	24	682	228 (33.43)	23
	22367	14 (0.06)	7	236100	24 (0.01)	5	26	6 (23.08)	4
	53325	20 (0.04)	5	642528	151 (0.02)	16	38	38 (100.00)	0
	127917	144 (0.11)	50	856246	444 (0.05)	10	437	78 (17.85)	5
	25850	5 (0.02)	1	170125	29 (0.02)	3	44	8 (18.18)	0
	140599	121 (0.09)	24	1204881	557 (0.05)	20	798	218 (27.32)	10
	78336	32 (0.04)	10	450637	91 (0.02)	7	119	38 (31.93)	4
	95167	35 (0.04)	6	889859	223 (0.03)	10	164	91 (55.49)	2
Wales									
	69635	39 (0.06)	5 (0.01)	396593	181 (0.05)	9	74	11 (14.86)	0
	69635	39 (0.06)	5	396593	181 (0.05)	9	74	11 (14.86)	0
Northern Ireland									
	51449	20 (0.04)	2 (0.00)	256140	83 (0.03)	1	111	68 (61.26)	2
	51449	20 (0.04)	2	256140	83 (0.03)	1	111	68 (61.26)	2
Channel Isles & Isle of Man									
	2021	8 (0.40)	3 (0.15)	31076	25 (0.08)	1	19	13 (68.42)	2
	518	3 (0.58)	2	7641	8 (0.10)	1	5	5 (100.00)	2
	531	3 (0.56)	1	10318	13 (0.13)	0	8	6 (75.00)	0
	972	2 (0.21)	0	13117	4 (0.03)	0	6	2 (33.33)	0
Republic of Ireland									
	72422	28 (0.04)	4 (0.01)	579187	166 (0.03)	16	66	57 (86.36)	0
	20695	6 (0.03)	0	149737	26 (0.02)	2	10	10 (100.00)	0
	51727	22 (0.04)	4	429450	140 (0.03)	14	56	47 (83.93)	0
Total	1304917	986 (0.08)	190 (0.01)	10133051	3939 (0.04)	150	4738	1394 (29.42)	65
Frequency of confirmed positive			1 in 6,868			1 in 67,554			

1. Donors being monitored because of previously reactive, but not confirmed positive, donations.

2. More information about confirmed positive infections will be reported in a quarterly surveillance report.

NATIONAL BLOOD SERVICE

INFECTION SURVEILLANCE

SIX MONTHLY INFECTION SURVEILLANCE REPORT - NO. 10

OCTOBER 1995 - JUNE 1999

DATA AT 31 December 1999

If you have any questions about the data in this report please contact Kate Soldan (NBA/PHLS-CDSC Infection Surveillance Officer) on 0181 200 6868 Extn. 4602

NOTES

This report is a tabular (and graphical) summary of the data submitted to the NBA/PHLS CDSC infection surveillance system by the end of December 1999 about infections detected from October 1995 to June 1999. Effort has been made to avoid errors or inaccuracies both within and between surveillance reports. However, the data sets are constantly being changed and updated as more information is reported and so minor inconsistencies between surveillance reports may arise.

Table 1 and Table 2 (denominators) contain data from the NBA/PHLS CDSC Donation Testing Surveillance data set. The information about cases that is summarised in Tables 2,3,4 and 5 is from the NBA/PHLS CDSC Infected Donor Surveillance data set at 31 December 1999 this data set consists of a sub-set of the infected donors identified by the Donation Testing Surveillance as not all infections had been reported in detail by the end of December 1999 (see Table 1). Table 6a contains both data specifically requested from blood centres at the end of 1995 about the total numbers of HCV positive new and repeat donors detected by the end of September 1995, and data from the NBA/PHLS CDSC Donation Testing Surveillance data set for October 1995 to June 1999. Table 6b contains data provided by the Scottish National Blood Transfusion Service Microbiology Reference Unit (SNBTS MRU) about the total numbers of HCV positive new and repeat donors detected in Scotland by the end of June 1999. Table 7 contains data from the NBA HIV Testing Surveillance database up to September 1995 (up to December 1995 for Scottish blood centres) and from the SNBTS MRU and the NBA/PHLS CDSC Donation Testing Surveillance data set from October 1995 to June 1999. Table 8 contains data about HBsAg testing of blood donations from the SNBTS MRU and the NBA/PHLS CDSC Donation Testing Surveillance data set from October 1995 to June 1999. Tables 9 and 10 contain information from the NBA/PHLS CDSC Post-Transfusion Infection Surveillance data set.

The Donation Testing Surveillance data classifies donors as new or repeat donors according to definitions used at blood centres. Information about the testing of previous donations is reported to the surveillance centre on the Infected Donor report: this allows classification of positive donors as newly-tested or previously-tested donors. Previously-tested donors may have been found to be positive, or indeterminate, on previous donations: they are not all donors who have seroconverted for the marker since their previous donation. The following definitions therefore apply to the terms used in this report.

New	A new donor by blood centre classification
Newly-tested	A donor who has not been previously tested for the marker under consideration by the blood transfusion services included in this surveillance.
Repeat	A repeat donor by blood centre classification
Previously-tested	A donor who has been previously tested for the marker under consideration by blood transfusion services included in this surveillance.

For citation of the data included in this report the following is suggested; "NBA/PHLS CDSC Unpublished Quarterly Infection Surveillance Report No.10, June 1999."

All tables contain data from the blood centres of England, Wales, Northern Ireland, The Republic of Ireland, the Channel Isles and the Isle of Man unless otherwise stated.

The next infection surveillance report will present data about donation collected up to 31 December 1999, and will include information about infection that is reported to the surveillance centre by 30 June 2000.

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Table 6a. **HCV infected blood donations: England & Wales**
Donations collected from 01/09/1991 to 30/06/1999

	New donors			Repeat donors[1]			Total		
	HCV infected	Donations tested	Rate per 100,000	HCV infected	Donations tested	Rate per 100,000	HCV infected	Donations tested	Rate per 100,000
1991 Sep-Dec	94	105,204	89.35	438	703,194	62.29	532	808,398	65.81
1992	289	303,597	95.19	518	2,190,696	23.65	807	2,494,293	32.35
1993	252	292,862	86.05	204	2,233,679	9.13	456	2,526,541	18.05
1994	254	313,363	81.06	125	2,209,965	5.66	379	2,523,328	15.02
1995	249	305,782	81.43	105	2,198,658	4.78	354	2,504,440	14.13
1996	191	296,156	64.49	72	2,243,229	3.21	263	2,539,385	10.36
1997	172	281,096	61.19	64	2,389,190	2.68	236	2,670,286	8.84
1998	117	266,540	43.90	67	2,235,443	3.00	184	2,501,983	7.35
1999 Jan-Jun	82	152,914	53.62	17	1,135,825	1.50	99	1,288,739	7.68
Total	1,700	2,317,514	73.35	1,610	17,539,879	9.18	3,310	19,857,393	16.67

[1] Including repeat donors newly tested for HCV infection.

Figure 6a. **HCV infected blood donations: England & Wales**
Donations collected from 01/09/1991 to 30/06/1999

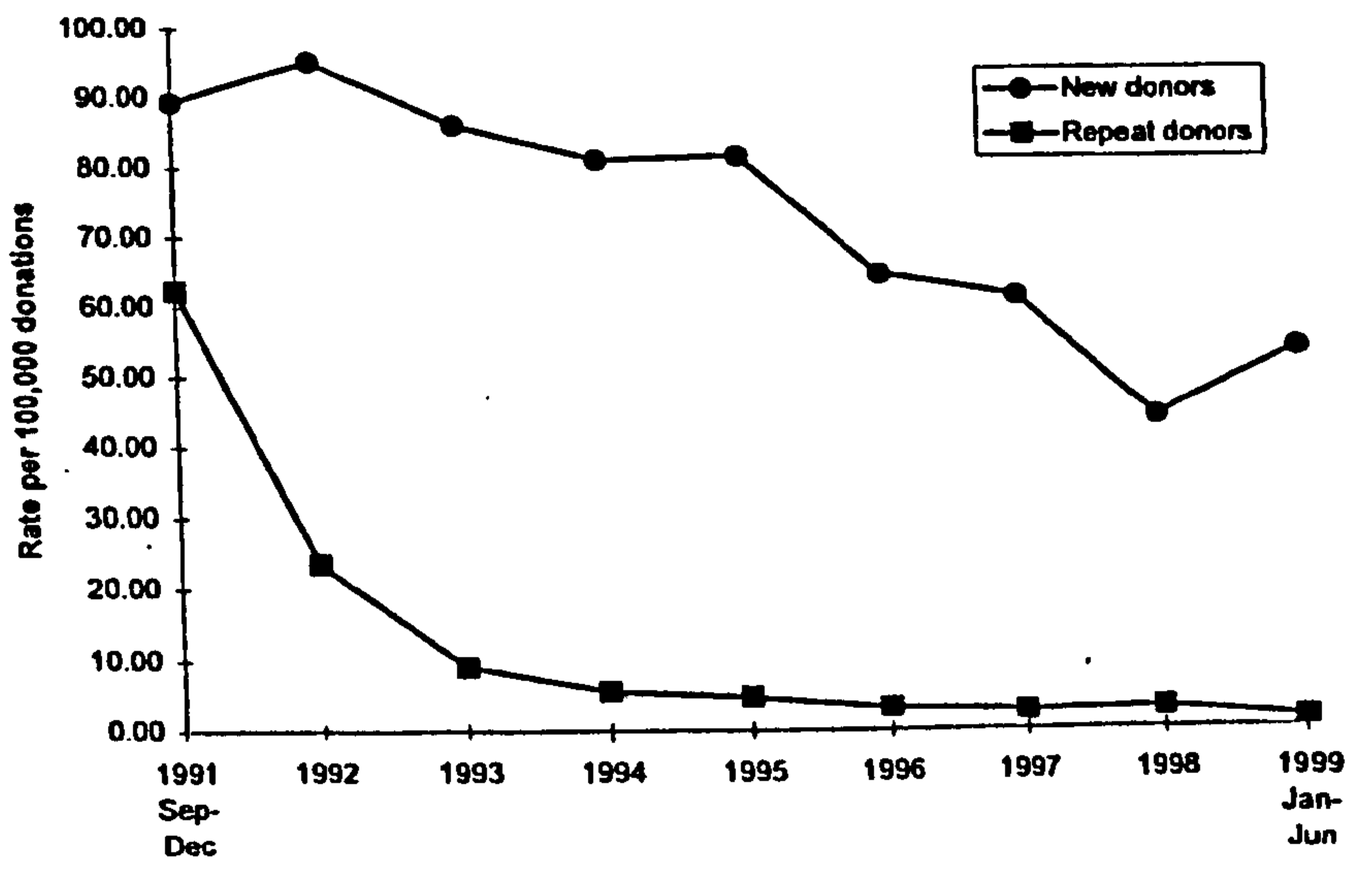


Table 6b. **HCV infected blood donations: Scotland**
Donations collected from 01/09/1991 to 30/06/1999

	New donors			Repeat donors[1]			Total		
	HCV infected	Donations tested	Rate per 100,000	HCV infected	Donations tested	Rate per 100,000	HCV infected	Donations tested	Rate per 100,000
1991 Sep-Dec	33	12,935	255.12	66	96,646	68.29	99	109,581	90.34
1992	55	34,879	157.69	102	297,946	34.23	157	332,825	47.17
1993	30	31,149	96.31	60	281,053	21.35	90	312,202	28.83
1994	25	29,396	85.05	39	283,313	13.77	64	312,709	20.47
1995	49	29,778	164.55	20	274,952	7.27	69	304,730	22.64
1996	34	29,905	113.69	19	270,782	7.02	53	300,687	17.63
1997	40	29,968	133.48	20	263,700	7.58	60	293,668	20.43
1998	31	28,667	108.14	13	256,438	5.07	44	285,105	15.43
1999 Jan-Jun	15	16,605	90.33	6	124,482	4.82	21	141,087	14.88
Total	312	243,282	128.25	345	2,149,312	16.05	657	2,392,594	27.46

[1] Including repeat donors newly tested for HCV infection.

Figure 6b. **HCV infected blood donations: Scotland**
Donations collected from 01/09/1991 to 30/06/1999

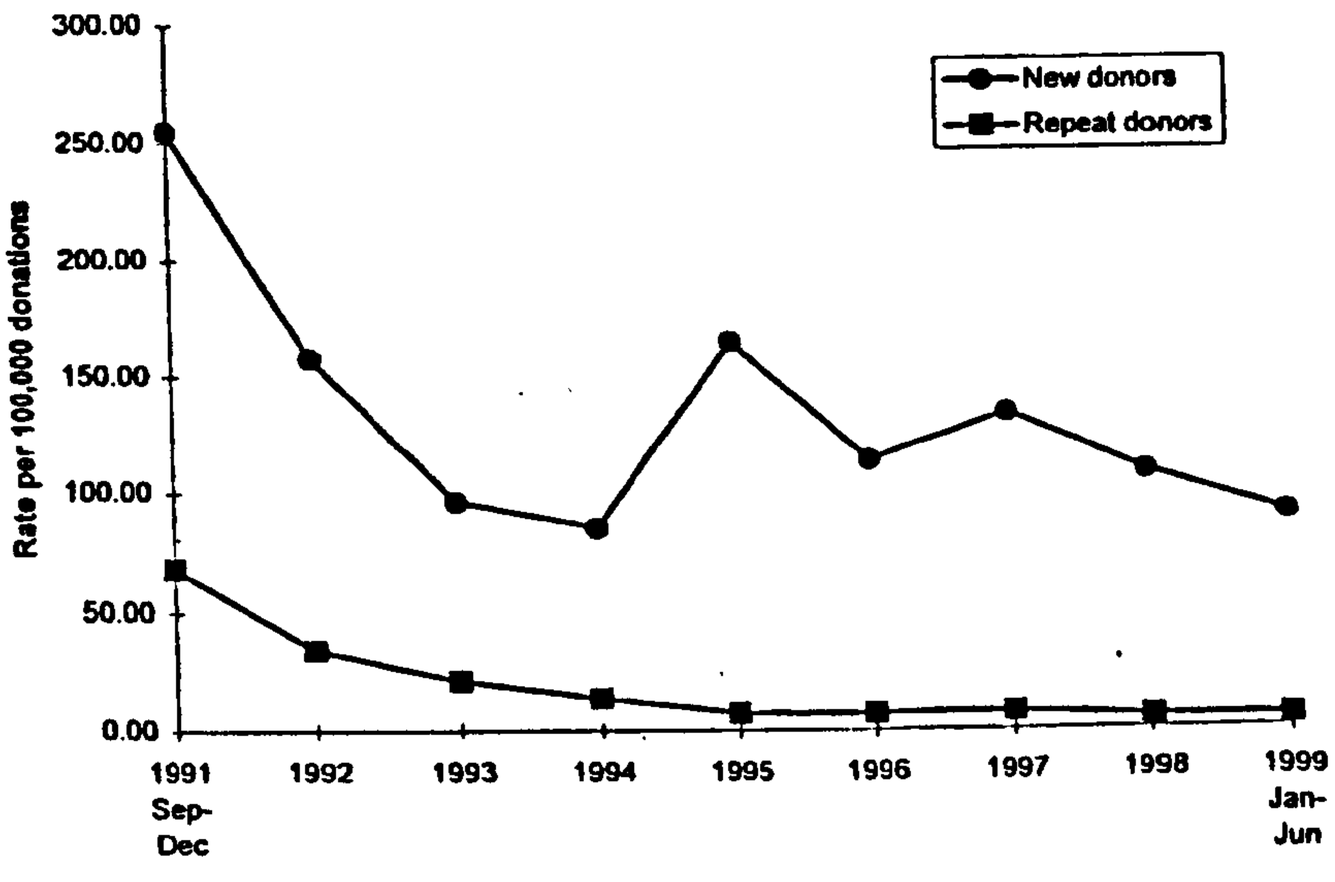


Table 7. **HIV infected blood donations: UK (i.e.England, Wales, Northern Ireland & Scotland)**
Donations collected from 01/10/1985 to 30/06/1999

	New donors			Repeat donors[1]			Total		
	HIV infected	Donations tested	Rate per 100,000	HIV infected	Donations tested	Rate per 100,000	HIV infected	Donations tested	Rate per 100,000
1985 Oct-Dec	5	-	-	8	-	-	13	610,918	2.13
1986	20	322,490	6.20	33	2,312,765	1.43	53	2,635,255	2.01
1987	12	340,770	3.52	11	2,246,471	0.49	23	2,587,241	0.89
1988	8	353,834	2.26	15	2,278,553	0.66	23	2,632,387	0.87
1989	17	372,748	4.56	20	2,368,391	0.84	37	2,741,139	1.35
1990	18	353,456	5.09	14	2,463,339	0.57	32	2,816,795	1.14
1991	16	442,692	3.61	15	2,506,550	0.60	31	2,949,242	1.05
1992	12	349,204	3.44	14	2,551,885	0.55	26	2,901,089	0.90
1993	11	333,574	3.30	9	2,581,492	0.35	20	2,915,066	0.69
1994	10	351,603	2.84	6	2,558,643	0.23	16	2,910,246	0.55
1995	17	352,229	4.83	13	2,548,813	0.51	30	2,901,042	1.03
1996	10	335,714	2.98	12	2,579,182	0.47	22	2,914,896	0.75
1997	22	319,609	6.88	10	2,720,413	0.37	32	3,040,022	1.05
1998	10	309,460	3.23	13	2,555,023	0.51	23	2,864,483	0.80
1999 Jan-Jun	6	178,746	3.36	5	1,288,482	0.39	11	1,467,228	0.75
Total	194	4,716,129	4.01	198	33,560,002	0.57	392	38,887,049	1.01

[1] Including repeat donors newly tested for HIV infection.

Figure 7.

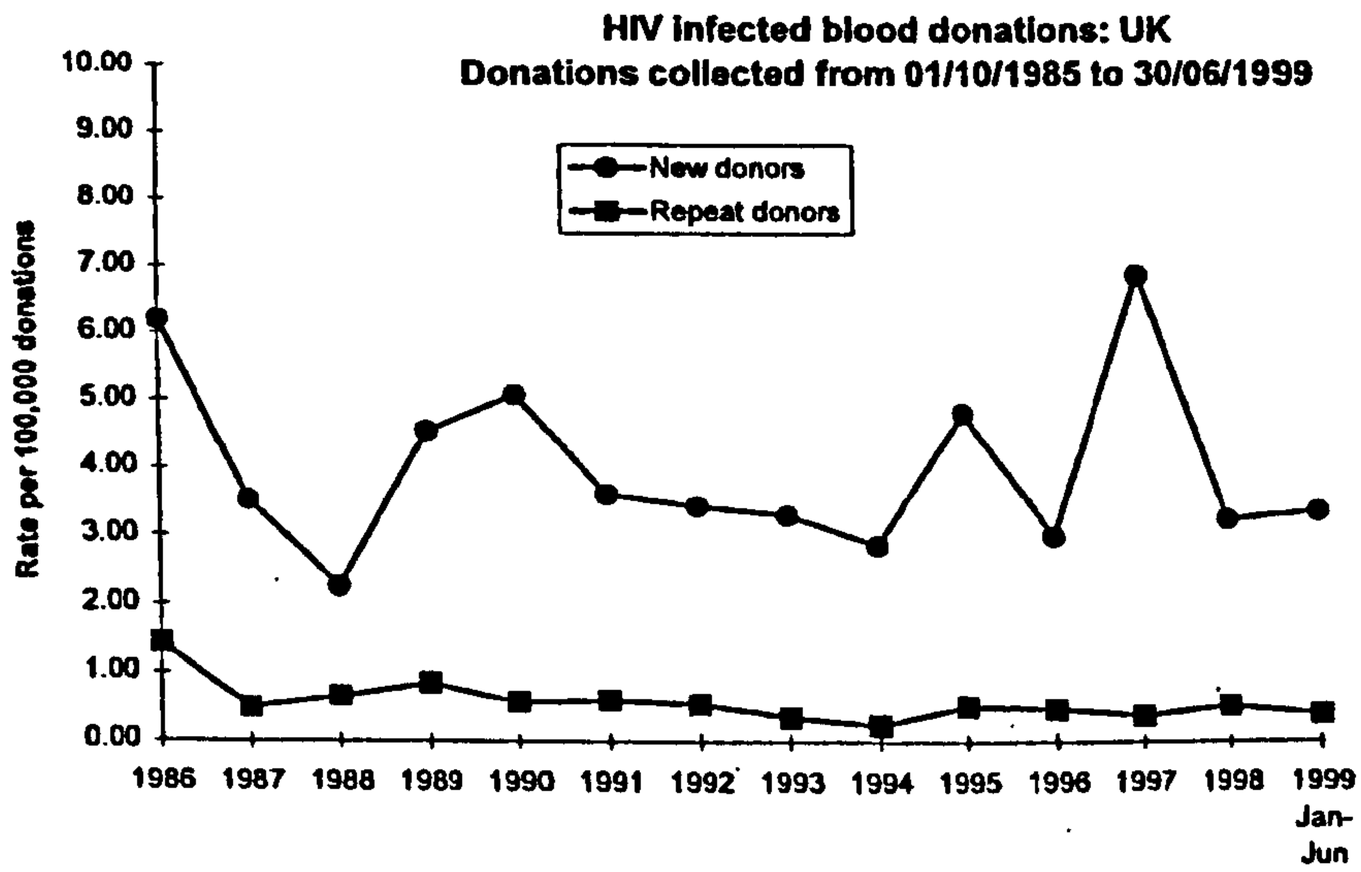
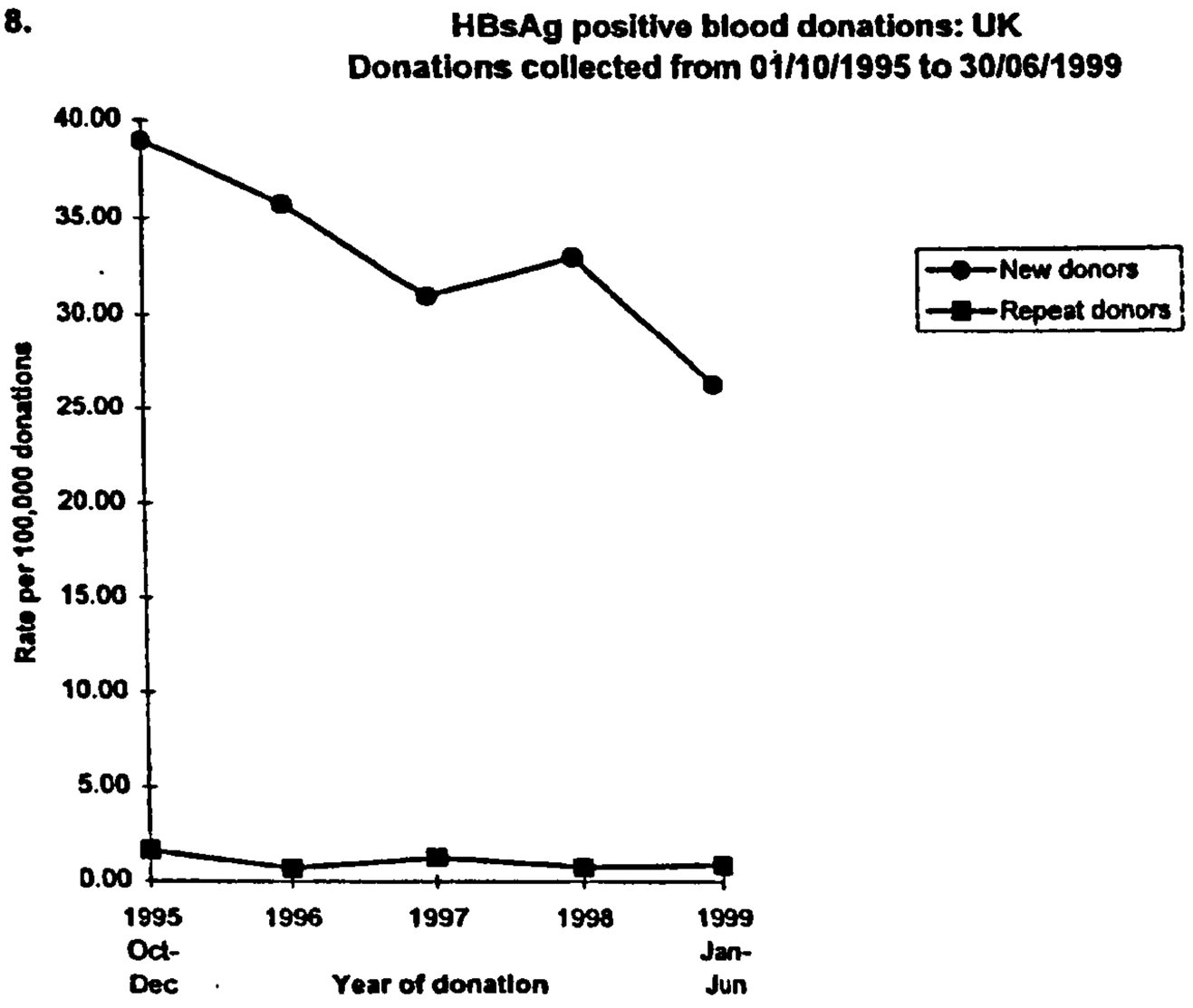


Table 8. HBsAg positive blood donations: UK (i.e.England, Wales, Northern Ireland & Scotland): 01/10/1995 to 30/06/1999

	New donors			Repeat donors[1]			Total		
	HBsAg positive	Donations tested	Rate per 100,000	HBsAg positive	Donations tested	Rate per 100,000	HBsAg positive	Donations tested	Rate per 100,000
1995 Oct-Dec	35	89,840	38.96	10	601,032	1.66	45	690,872	6.51
1996	120	335,714	35.74	18	2,579,182	0.70	138	2,914,896	4.73
1997	99	319,609	30.98	35	2,720,413	1.29	134	3,040,022	4.41
1998	102	309,460	32.96	19	2,555,023	0.74	121	2,864,483	4.22
1999 Jan-Jun	47	178,746	26.29	11	1,288,482	0.85	58	1,467,228	3.95
Total	403	1,233,369	32.67	93	9,744,132	0.95	496	10,977,501	4.52

[1] Including repeat donors newly tested for HBsAg.

Figure 8.



Note: Prior to October 1995, HBsAg positive donors were reported to North London blood centre.

brillate) have been challenged.[5] Trained doctors can do all those things. Doctors also have an advantage in that they are allowed to give thrombolytic treatment, which improves the outcome of patients who have had heart attacks.[6] The relative advantages of different staff is unclear in the case of trauma,[7] and two American studies have shown that patients with penetrating injuries attended by either the police[8] or the public [9] had as good or a better outcome than those attended by trained ambulance crews. Patients with severe head injuries often need to be paralysed and ventilated, which usually can be undertaken only by doctors.[10]

The research is inconclusive, but well trained doctors undoubtedly have a role in prehospital emergency care. Yet undergraduate medical training is poor preparation, and that is why the Royal College of Surgeons has established a specialist examination in prehospital care. BASICS also offers training and has proposed a system of accreditation so that ambulance services can be sure that doctors are adequately trained. The new faculty is open to doctors, ambulance staff, nurses, first aiders, and others interested in prehospital care, and undoubtedly this difficult work needs teamwork. The roles of first aider, ambulance person, and doctor are complimentary.

Research is lacking not only on who should deliver care but also on the best care to offer. Guidelines cannot be automatically transposed from hospital practice to emergency prehospital care. An important element of all prehospital work is the decision of when to transport the patient. Will an intravenous infusion help an exsanguinating patient or simply delay definitive treatment by a surgeon? Giving fluid to patients with blunt chest trauma before transport to hospital increases mortality,[11] as does delaying the transfer to hospital of patients with penetrating trauma in order to wait for the arrival of paramedics.[12] Some types of care can be given safely only in hospital.

Further research is also needed on the best equipment for prehospital emergency care. Some forms of equipment—for instance, extrication devices—are unique to prehospital care, and they have not been adequately assessed. Some equipment may worsen the patient's predicament: pneumatic antishock garments may increase mortality, probably because they compromise respiratory function[13]; and semirigid collars used for immobilising the neck may raise intracranial pressure (G Davies, personal communication). New forms of telemetric equipment are also being proposed that will allow doctors to assist from a remote location. Their use will need evaluation and audit.

The research and audit that are necessary to underpin prehospital emergency care will appear in the new journal . A new body has been proposed to regulate paramedics, and the new faculty is collaborating with BASICS on training and accreditation. All the professional groups need to work together, and the journal will be for them all. These initiatives should ensure better outcomes for patients who need emergency care.

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* For details of the new journal see the advertisement facing p 1241 (Clinical Research edition), p 1253 (General Practice) and p 1243 (International), and information on the BMJ homepage on the World Wide Web (http://www.bmj.com/bmj/).

A SHOT in the arm for safer blood transfusion

A new surveillance system for transfusion hazards

How safe is blood transfusion in 1996? Despite recent publicity surrounding contaminated blood bags and hepatitis C virus, it is probably safer than it has ever been. More rigorous donor selection, improved viral screening tests, tighter quality control, and accreditation of hospital laboratories have all played a part. But there is no room for complacency. As was highlighted by an editorial in the *BMJ* two years ago, preventable deaths after transfusion still occur.[1]

The commonest cause of transfusion related death in the United States, where reporting to the Food and Drugs Administration is mandatory, is the transfusion of ABO incompatible blood.[2] A British survey revealed that episodes where wrong blood is given to a patient as a result of poor patient identification may complicate as many as 1 in 30 000 transfusions.[3] Mortality is minimised, firstly, because the distribution of blood groups in the British population means that two thirds of "wrong" transfusions are by chance ABO compatible and, secondly, by the fact that only 1 in 10 ABO incompatible transfusions is fatal.[4] Nevertheless, such episodes, and other near miss events, reveal serious deficiencies in the transfusion process. Rarer immunological complications such as transfusion associated graft versus host disease [5] and transfusion related lung injury [2] also continue to cause fatalities.

What is the situation with transfusion transmitted infection? Recent American figures suggest that the risk from a donor who is infectious but not yet seropositive is about 1 in 500 000 for HIV, 1 in 100 000 for hepatitis C virus, and 1 in 60 000 for hepatitis B virus.[6]

Recent calculations for England suggest even greater safety than in the United States, with estimated current risks of HIV and hepatitis C infectious donations entering the blood supply for any reason of 1 in more than 2 million and 1 in more than 200 000 respectively (K Soldan, JAJ Barbara, unpublished

data). Estimates of risk for hepatitis B infection are complicated by the fact that transmission may arise from donors with chronic hepatitis B infection and undetectable hepatitis B surface antigen. In Britain, there has been only one reported case of HIV transmission from the 26 million units of blood tested since 1985.[7] Rare cases of fatal bacterial contamination of blood also occur,[8] and there has been at least one probable transmission of human T cell leukaemia/lymphoma virus type I by transfusion in Britain.[9]

Unlike the United States, Britain has had no system for comprehensive monitoring of transfusion hazards. Because blood is not a licensed product, the Committee on the Safety of Medicines' yellow card system covering serious reactions to drugs and plasma fractions such as factor VIII has never included whole blood or its components (red cell concentrates, platelets, fresh frozen plasma, and cryoprecipitate). This gap in reporting is now being filled, with the recent launch of the serious hazards of transfusion (SHOT) initiative. Covering the whole of Britain and the Republic of Ireland, the initiative is a voluntary and confidential reporting system for transfusion related deaths and other serious complications. It covers all infectious and major immunological complications of transfusion, as well as all episodes where wrong blood is given, whether or not the patient is harmed. Complications of autologous donation will also need to be reported, since both bacterial contamination[10] and errors in administration[11] have been described.

SHOT aims to improve transfusion safety further by analysing reported information on transfusion hazards and translating the findings into transfusion service policy, clinical guidelines, and training. Similar systems already exist for confidential reporting of maternal, infant, and perioperative deaths, and their value is widely appreciated.

The success of the scheme will depend on the participation of all staff administering blood, so its activities are being directed by a steering group with wide representation from royal colleges and professional bodies. The system will be confidential, with no possibility of identifying patients or hospitals from the final data set. The need for anonymity is paramount to encourage reporting without prejudice to the individuals or institution concerned.

Hospital haematologists responsible for transfusion will have a key role in reporting both infectious and non-infectious hazards. Blood transfusion centres should be rapidly informed about possible viral or bacterial transmissions so that withdrawal of other components and appropriate investigations can begin. Vigilance of reporting of infections to national surveillance centres also continues. Full details of the SHOT scheme, along with the clinical features of the serious complications of transfusion, are described in the recently revised *Handbook of Transfusion Medicine*, provided free to all hospitals.[12]

One example is given to indicate the potential value of the scheme. In 1994, a report was published of three cases of transfusion associated graft versus host disease linked to a new purine antagonist, fludarabine, under trial for chronic lymphocytic leukaemia.[13] During the preparatory period for the launch of SHOT, one of us (LMW) was made aware of three further cases from different parts of the country.[5] As a result, national guidelines now recommend the use of gamma irradiated components to prevent transfusion associated graft versus host disease in patients who receive fludarabine.

Transfusionists face many challenges in today's health service. There are many additional but costly testing and processing manoeuvres to which donated blood could be subjected, but which of these would best improve transfusion safety? Should we be testing for additional viral markers such as antibodies to hepatitis B core antigen and human T cell leukaemia/lymphoma virus, moving to virally inactivated fresh frozen plasma, or undertaking leucocyte depletion of all blood collected? Or would the public be better served by extensive investment in quality assurance and audit of transfusion practice,[15] accreditation of "transfusion prescribers,"[16] basic research into blood and plasma substitutes, or widespread provision of facilities for autologous transfusion?

The SHOT initiative has the potential to provide the data necessary to inform these kinds of decision. Its success will depend on good case ascertainment, which will require vigilance and support from all staff who care for transfusion recipients. We thank Dr John Barbara for invaluable advice and discussions on infection risk.

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plasma (Table 1). Our PCR results for HCV RNA were confirmed independently for all 14 negative lot samples and for 12 (85.7%) of 14 PCR-positive lot samples (John Saldanha, PhD, National Institute for Biological Standards and Control, Potters Bar, UK). The viral load for 30 HCV RNA-positive lot samples was compared to that of the National Institute for Biological Standards and Control reference preparation number 95/590, which had been validated by international collaborative studies to contain approximately 4000 copies of HCV RNA per mL. This reference preparation is expected to test positive after a single PCR amplification. Twenty-eight of the 30 lots tested negative after the first amplification; therefore, they contained less than 4000 copies of HCV RNA per mL.

On the basis of these findings, we believe that screening for anti-HCV has reduced the viral load to concentrations so low that the manufacturing process itself makes HCV RNA undetectable in the finished product. Nevertheless, as an additional measure to ensure the viral safety of these products, we strongly recommend accelerating the introduction of a virus-inactivation and/or -removal step in the preparation of all IMIG products.

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Unexplained hepatitis C virus antibody seroconversion in established blood donors

In two articles published in the Journal of Medical Virology[1] and **TRANSFUSION**,[2] Atrah et al. report hepatitis C virus (HCV) seroconversion in 10 blood donors whose blood was collected by the Birmingham (UK) Blood Centre from 1992 through 1995. We believe that the reports by Atrah et al. overestimate the incidence of HCV seroconversion in a representative English blood donor population, because their findings are inconsistent with a significantly larger and contemporaneous national survey, and because their corroborating evidence of HCV infection is inconclusive.

A retrospective national survey of blood donors who had seroconverted for HCV between January 1993 and December 1995 has been conducted in England (Soldan K, et al. HCV seroconversions in blood donors: England, 1993 to 1995. Manuscript submitted for publication). The case definition used for this survey required the demonstration of a change from negative results to positive results on comparable enzyme immunoassay and recombinant immunoblot assay. From 1993 through 1995, 14 cases of HCV seroconversion in blood donors were recorded by the English survey (including Donor 2 from Atrah et al.[1]). Six of the cases described by Atrah et al. (Donors 1 and 3 from the first article and Donors 1 to 4 from the second article) did not satisfy the case definition (based on serologic test results) used for this survey. These six donors also had characteristics that make us doubt the authenticity of seroconversion for HCV in them: they differ from the accepted cases with respect to age, relevant risk factors, and polymerase chain reaction (PCR) results.

The mean age of the English survey donors was 30 years (22- 43) compared to 52 years (38-64) for the donors presented by Atrah et al. ($p<0.001$). Fifty percent (6/12) of the national survey donors for whom exposure history information was available had had a probable exposure to HCV during the relevant period (2 had injected drugs, 2 had HCV-infected sexual partners, 1 had a sexual partner who had injected drugs, and 1 had blood contact during a fight). None of the donors presented by Atrah et al. had a known probable exposure to HCV infection. For 3 of the 4 donors in the Atrah study for whom a PCR test result was available for the first seropositive donation, no HCV RNA was detected: all 3 donations were taken less than 1 year after the last seronegative donation. Only 1 of 1 0 English survey donors with a PCR test performed at the time of the first seropositive donation was PCR negative: this donation was taken 2 years after the last seronegative donation. Similarly, only 1 of the 6 HCV seroconversions recorded in Scotland during this period was in a donor who was PCR negative at the first seropositive donation.

We also note here the lack of transmission of HCV by a donor (Donor 2 from Atrah et al.[2]) who is reported as being PCR positive on a donation dated September 1993, the recipient of which was identified, counseled, and found to be uninfected. This donor was found to be PCR negative 9 months later. This pattern of viremia and infectivity is unexpected and should be carefully confirmed, perhaps by retesting key samples in an independent laboratory, before its implications may be accepted.

LETTERS TO THE EDITOR

Atrah et al. report an HCV seroconversion incidence of 0.34 per 10,000 previously seronegative donors (1/30,000) in 1994. The denominator available for the national survey was donations from repeat donors, rather than the number of seronegative donors tested, which was used by Atrah et al. Use of this denominator produces a lower estimate of the seroconversion rate in repeat donors but still allows comparison between centers and periods. The extent of this underestimation in 1994 depends on how much less than 1 year the average interval between donations is; unless interdonation intervals vary considerably between blood centers, the comparison of rates using this denominator is valid. If we accept the validity of the cases presented by Atrah et al., the rate of postseroconversion donations in all donations from repeat donors in Birmingham during 1994, calculated by our method (0.17/10,000), is tenfold the analogous rate in the rest of England (0.016/10,000). If Birmingham and the rest of England have a common HCV seroconversion rate among repeat donors, the probability that such a high rate would be observed in the Birmingham survey is extremely low ($p = 0.004$). The observed annual rates of post-HCV seroconversion donations in England for the years 1993, 1994, and 1995 were 0.023, 0.014, and 0.028 per 10,000, respectively. The rate of HCV seroconversion in repeat blood donors in Scotland during this period was 0.06 per 10,000.

The differences in the results from the two surveys imply that different criteria were used for the ascertainment of cases of seroconversion. Other blood centers' underreporting of HCV seroconversions to the English survey or local factors affecting HCV transmission or donor selection in the Birmingham area could account for some of the differences. However, in the light of the analysis of the characteristics of these cases and bearing in mind our concerns about the confirmation of HCV antibody detection,[3] we consider the differences in the estimated seroconversion rates to be attributable to error in the ascertainment of seroconversion in the Birmingham survey.

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The above letter was sent to Atrah et al.; Dr. Atrah offered the following reply.

Hewitt et al. misrepresent our two articies.[1,2] We reported seroconversion in 7 blood donors, not 10. We reported seroconversion in 3 donors in the first article[1] and in 4 donors in the second.[2] Three additional donors were reported in the second article as an example of a change in serologic status that we did not consider sufficient to categorize as a documented seroconversion. This difference invalidates the subsequent calculations, comparisons, and conclusions of Hewitt et al.

The word seroconversion may legitimately convey a different meaning in different studies. Hewitt et al. may argue the merit of their definition as compared to ours, but they should not doubt our figures, which were derived by more accurate means and based on different criteria. Our studies relied on an active systematic search for donors who were found positive by defined criteria in two successive years after being tested negative by the same manufacturer's assay and generation of kit on previous donations in one regional transfusion center. Their means of case detection relied on notification of seroconversion by 14 regional transfusion centers using kits from different manufacturers and different confirmation algorithms. Furthermore, their criteria. for seroconversion were not explained to those filling out the forms; this could have affected the consistency of the information supplied.

Hewitt et al. make the assumption that seroconversion is synonymous with infection. We did not make such a claim, as we recognize that test systems have limitations that make such an assumption untenable. We reported seroconversion as we defined it and attempted to discuss its causes and implication in the light of available knowledge.

Finally, if Hewitt et al. consider our findings for HCV seroconversion in Birmingham excessive and unacceptable, they should also explain their own published data. I refer the reader to the report presented at the annual meeting of the

Reprinted from the **BMJ** *, 9 May 1998, Vol 316, p 1413-1417*

Papers

Incidence of seroconversion to positivity for hepatitis C antibody in repeat blood donors in England, 1993-5

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Abstract

Objective: To estimate the rate of seroconversion to positivity for hepatitis C antibody in repeat blood donors in England and to describe the probable routes of infection in these donors.

Design: Retrospective survey of blood donors becoming positive for hepatitis C antibody and of the results of donation testing.

Setting: The 14 blood centres in England.

Subjects: All repeat donors giving blood between January 1993 and December 1995.

Main outcome measures: Number of donors developing hepatitis C between donations during the three years of testing for hepatitis C antibody at English blood centres and the rate of seroconversion among repeat blood donors. Probable routes of infection.

Results: 14 donors during 1993-5 fulfilled the case definition for seroconversion to positivity for hepatitis C antibody. The estimated seroconversion rate for infection with hepatitis C in repeat donors was 0.26 per 100 000 person years (95% confidence interval 0.15 to 0.43). Counselling after diagnosis found that four of these donors had risk factors specified in the criteria excluding people from giving blood but these factors had not come to light before donation. Another of the donors who seroconverted had a risk factor that has since been included in the exclusion criteria. Heterosexual intercourse was considered to be the most likely route of infection for five of the 14 donors.

Conclusions: The rate of seroconversion for positivity to hepatitis C antibody in repeat blood donors in England was extremely low. During 1993-5 fewer than 1 in 450 000 donations were estimated to have come from repeat donors who had become positive for hepatitis C antibody since the previous donation.

Introduction

In September 1991 blood transfusion services in the United Kingdom began routinely testing all blood donations for antibody to hepatitis C virus. Since then around 2 million healthy adults have been tested for the antibody each year by the English national blood service. National collation of test results and of characteristics of donors positive for hepatitis C antibody provides valuable information about donors and about a selected sample of the adult population of England.

Most acute infections with hepatitis C are asymptomatic, and most probably pass undetected. Recent infection is implied when a donation that is positive for hepatitis C antibody was preceded by a donation that was negative for the antibody. The testing of donations from repeat donors therefore provides a rare opportunity to identify incident infections with hepatitis C virus. Information about incident infections is of interest to blood transfusion services and to public health workers as it relates to current rather than past transmission of the virus. The selection process for blood donors aims to exclude donors who have recognised risks of contracting bloodborne infections. Incident infection in blood donors usually indicates one of three things: a failure in the definition or application of selection criteria; an unrecognised exposure to bloodborne infection; or infection through an exposure that is not included in the selection criteria because it is common in blood donors and thought to be associated with a comparatively small risk of infection. There remains a small risk of transmission of hepatitis C virus by transfusion from the infectious donations of donors who are negative for hepatitis C antibody and from failures in the testing and exclusion of donations that are positive for the antibody. The number of donors who seroconvert between donations is needed to estimate the risk of collecting a donation from a recently infected donor who has not yet developed detectable hepatitis C antibodies and hence the risk of transmitting hepatitis C by transfusion.

During 1994-5 we surveyed seroconversions to hepatitis C antibody detected by English blood centres from September 1991 to December 1995. We used these results with data from the infection surveillance system of the National Blood Authority and Public Health Laboratory Service Communicable Disease Surveillance Centre to estimate the rate of seroconversion to positivity for hepatitis C antibody in repeat donors in England during 1993-5.

Subjects and methods

Sample

Blood donations in England are obtained from voluntary unpaid donors. The selection procedure excludes people who are outside the age range 18-65 years, those who have been at known high risk of contracting

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BMJ 1998;316:1413–7

bloodborne infections, and those who have any medical condition which contraindicates either the loss of 450 ml of blood or the giving of their blood to patients. The number of repeat donors in 1994 constituted around 4% of the population aged 18-65 in England in the middle of 1994.

During the study all donations were tested for hepatitis C antibody using enzyme linked immunosorbant assays (ELISAs). Initially reactive donations were retested by ELISA. Donations that were reactive on repeat testing were not used, and supplementary tests (additional ELISAs and recombinant immunoblot assay and, in some cases, the polymerase chain reaction for hepatitis C DNA) were performed on them to clarify the infection status of donors.

Donors with evidence of infection with hepatitis C virus were contacted by the blood centres and offered additional testing and counselling by the blood centre, with referral to a relevant medical specialist, or they were referred to their general practitioner for further management.[1] Risk factors for hepatitis C were discussed with donors during their follow up and any acknowledged by the donor were recorded.

Case definition

A standardised algorithm for confirmatory testing of blood donations had not been used, and we had to accommodate variation in the tests used. We used a comprehensive case definition that was designed to include all true biological seroconversions and exclude false positive results and any spurious results caused by changes in test format and performance over time.

The three case definitions were:

- Negative results in third generation recombinant immunosorbent assay in pre-seroconversion donation and positive results in third generation recombinant immunosorbent assay in post-seroconversion donation, without negative results in polymerase chain reaction for hepatitis C DNA for the post-seroconversion donation if given <12 months after the pre-seroconversion donation
- Negative results in ELISA and second generation recombinant immunosorbent assay in pre-seroconversion donation and positive results in ELISA (of same manufacturer and generation as pre-seroconversion test) and second generation recombinant immunosorbent assay in post-seroconversion donation, without negative results in polymerase chain reaction for hepatitis C DNA for the post-seroconversion donation if given <12 months after the pre-seroconversion donation
- Negative results in third generation ELISA in pre-seroconversion donation and positive results in third generation ELISA and recombinant immunosorbent assay in post-seroconversion donation, without negative results in polymerase chain reaction for hepatitis C DNA for the post-seroconversion donation if given <12 months after the pre-seroconversion donation.

Methods

In July 1994 all English blood centres were asked to return information about the tests performed and results obtained on the first donation positive for hepatitis C antibody (post-seroconversion donation) and the last donation negative for hepatitis C antibody (pre-seroconversion donation) for each donor who was considered to have seroconverted between donations since testing began in 1991. Seroconversions identified after July 1994 were also reported and included in the survey. Information was also requested about possible exposures to hepatitis C virus. In October 1995 the national system for the surveillance of donation testing was revised and seroconversions were then identified from routine surveillance reports.

Test results were examined to see whether they met the case definition. If they did not the reporting blood centre was contacted and asked for any additional test results or to perform additional tests on archived samples. Most commonly they were asked to perform parallel recombinant immunoblot assays on samples of pre-seroconversion and post-seroconversion donations. Follow up of missing returns and requests for additional information continued during 1995.

During 1991 (September-December) and 1992 most repeat donors tested for hepatitis C antibody were being tested by the National Blood Service for the first time. As a previous negative result on testing for hepatitis C antibody test is a prerequisite for seroconversion to positivity for hepatitis C antibody, rates for 1991 and 1992 were not calculated.

The rate of post-seroconversion donations in all donations from repeat donors was calculated by dividing the number of seroconversions by the number of donations from repeat donors. The number of donations from repeat donors tested for hepatitis C antibody during 1993, 1994, and 1995 was obtained from the national system for the surveillance of donation testing. The incidence of seroconversion was calculated by dividing the number of seroconversions by the number of person years at risk. The number of person years was estimated by dividing the number of donations from repeat donors by the average annual number of donations per repeat donor. The average number of donations per repeat donor at one blood centre (which tests 5% of the repeat donor donations in England) was 1.71 over one year and 3.49 over three years (1993-5). The average annual number of donations during the three years from 1993 to 1995 was therefore taken as 1.16 (3.49/3). This is equivalent to an average interval between donations of 0.86 years.

Results

We received 23 reports of putative seroconversion in repeat donors tested between September 1991 and the end of 1995. The test results available for seven of them did not satisfy the case definition. We asked centres to report on only the donors for whom full testing information was available, so these seven reports do not represent all the possible additional cases of recent infection with hepatitis C virus in repeat donors in whom the data are insufficient to satisfy our case definition. Two of the donors who fulfilled the case definition received their diagnosis during 1991 or 1992, and 14 of the cases were diagnosed during the study years, 1993-5 (table 1). The difference in the rates for 1993, 1994, and 1995 was not significant (P = 0.59). Results from the polymerase chain reaction were available for 10 of the 14 donors: nine donors had positive results and one donor, whose first seropositive donation was

Table 1 Seroconversion to positivity for hepatitis C antibody among repeat donors in England, 1993-5

	1993	1994	1995	1993-5
No of donations from donors who had seroconverted since previous donation	5	3	6	14
No of donations from repeat donors tested for antibody to hepatitis C virus	2 140 712	2 116 178	2 105 038	6 361 928
Frequency of donations from donors who had seroconverted since previous donation	1 in 428 142	1 in 705 393	1 in 350 840	1 in 454 423
Rate of seroconversion per 100 000 person years (95% CI)	0.40 (0.17 to 0.96)	0.24 (0.08 to 0.75)	0.49 (0.22 to 1.08)	0.26 (0.15 to 0.43)

Table 2 Acknowledged probable exposure to hepatitis C virus in 14 repeat donors who became positive for hepatitis C antibody

Probable exposure to hepatitis C virus	Criterion for exclusion of blood donation in 1995	No of seroconverting donors		
		Total (n=14)	Men (n=8)	Women (n=6)
Injecting drug use	Yes	2	2	0
Heterosexual intercourse		5	1	4
Partner with hepatitis C*	Yes	1	1	0
Partner who injected drugs†	Yes	2	0	2
Partner with tattoos	No	1	0	1
Partner from country with high prevalence of hepatitis C	No	1	0	1
Blood contact with person with risk factors	No	1‡	1	0
None identified	No	4	2	2
No information		2	2	0

*At time of donation this selection criterion was not in use.[2]
†In one case, partner was found positive for antibody to hepatitis C after donor was given diagnosis; in other, antibody status of partner was not known.
‡Also reported on in Atrah et al.[3]

taken two years after the last seronegative donation, had negative results.

Five blood centres reported no seroconversions. Three centres reported more than one seroconversion; one centre in one of the Thames regions reported four cases and had the highest rate of seroconversion, and two centres, outside the Thames regions, reported two cases each. There was no significant heterogeneity between the rates by centre (deviance = 15.9, df = 13, P = 0.25).

The average interval between the pre-seroconversion and post-seroconversion donation for the 14 donors was 1.29 years (median 1.38 years, range 0.42-2.33 years). This interval was 1.5 times longer than the average interval in 1993-5 for all repeat donors.

Table 2 shows the reported probable exposures to infection of those who seroconverted (information about ethnic group was not gathered). The average age of all repeat donors was around 40. The mean age of the 14 donors who seroconverted was 30 years 6 months (95% confidence interval 26 years 7 months to 34 years 5 months); the mean age of the men was 31 years 5 months (26 years 1 month to 36 years 8 months) and of the women 29 years 4 months (21 years 1 month to 37 years 6 months).

Discussion

Estimating seroconversion rates

A total of 412 repeat donors who were positive for hepatitis C antibody were identified by English blood centres during 1993-5. Only 14 of them were proved to be incident infections with hepatitis C virus. This survey estimates the minimum rate of seroconversion to positivity for hepatitis C antibody in repeat donors in England during 1993-5. Our case definition excluded spurious seroconversion due to changes in test format and performance. The sensitivity and specificity of ELISAs and recombinant immunoblot assays used to test for hepatitis C antibody changed between 1991 and 1995, and third generation tests were introduced during 1993. By the time of this survey many of the archived samples from the pre-seroconversion donations under investigation had been used for repeat and supplementary tests or had been discarded, depending on each blood centre's protocol. Therefore, repeat and supplementary testing of pre-seroconversion donations was limited. Because we required evidence of comparably confirmed negativity for the last seronegative donation, we may have excluded some cases of true seroconversion. Previous reports of seroconversion to positivity for hepatitis C antibody with less strictly applied case definitions[4] have been justifiably challenged,[5] and we chose to identify clear cut rather than probable cases. Also, our survey was retrospective and relied on retrieval of blood centres' records of tests performed up to four years previously. For these reasons, this study may underestimate the number of donors who seroconvert and therefore the rate of seroconversion among repeat donors in England. Donations from repeat donors who were being tested for hepatitis C antibody by the national blood service for the first time during 1993-5 could not be excluded from the denominators that we used. A study conducted on donations during 1993 by one blood centre found 1.8% of donations from repeat donors to be from donors not previously tested for hepatitis C antibody by the blood centre.[6] This inaccuracy in our denominator is likely to result in a further, although slight, depression of the seroconversion rates as estimated from these data.

One blood centre has published reports about three cases diagnosed during 1993[3] and a further four cases diagnosed during 1994 and 1995[6] in which seroconversion was thought to have occurred. The blood centre obtained denominators of previously negative donors tested for hepatitis C antibody during 1993 and estimated the seroconversion rate during 1993 to be

2.78 per 100 000 (1 in 35 937) previously negative, repeat donors[5]: more than 10 times the estimate from our national study. However, the case definition used by this centre may have been flawed[7,8]; only one of the cases described satisfied the case definition that we used. We consider the estimate of the rate of seroconversion in repeat blood donors derived by this single centre to be erroneously high.

Key messages

- The rate of seroconversion for positivity to hepatitis C antibody in English blood donors is low—0.26 per 100 000 person years during 1993-5 (95% confidence interval 0.15 to 0.43)
- The probable route of infection was unknown in a third of the blood donors who seroconverted during 1993-5 and who provided information on risk factors
- The exclusion of blood donors with a history of probable exposure to hepatitis C remains an important strategy to help keep the blood supply free of infection

Blood donor sample

Selection criteria for donors aim at selecting a sample of the population that does not report a recognised risk for bloodborne infections before donation.[9] Since the early 1980s potential donors have been given explanatory literature, and since 1989 all new donors and donors who have not attended for two years or more have been directly questioned about risk factors. One centre has additionally asked donors to complete a questionnaire. The procedure for eliciting information about exposures to risk of infection with hepatitis C virus from infected donors has varied throughout the United Kingdom. A standard questionnaire for interviewing donors is soon to be introduced. Information obtained after donation from infected donors may be affected by bias related to the interviewer and the donor. Most blood donors infected with hepatitis C virus have reported a history of injecting drug use,[10-13] typically many years before donating blood. Almost one third of those who seroconverted in this study had no risk factors for infection with hepatitis C virus identified by the blood service. Testing the sexual partners of donors who seroconverted may help to establish the true extent of heterosexual transmission in the donor population. Uncommon routes of transmission and possible exposures that are not thought to be associated with risk of infection with hepatitis C should also be investigated.

Seroconversion for hepatitis C virus among repeat blood donors in England is rare. This implies that the incidence of hepatitis C in the population represented by repeat blood donors is now low or that selection criteria for donation of blood effectively exclude most repeat donors with current exposure to hepatitis C virus. During 1993-5, 14 donations (less than 1 in 450 000 donations) were obtained from donors who had seroconverted for hepatitis C virus since a previous donation was negative for antibody. During the same period 15 donations were obtained from donors who had developed detectable HIV antibody since their previous donation. The number of repeat donors who become infected with hepatitis C virus or other bloodborne infections but do not return to donate after their seroconversion cannot be ascertained by donation testing. In the future, tests for nucleic acids may enable detection of infectious donations that test negative for antibody.

Recipients and new donors

We did not determine infection with hepatitis C virus in those who received the seronegative pre-seroconversion donations. Tracing recipients of potentially infectious donations is conducted by blood centres, and one of the 14 pre-seroconversion donations has been shown to have transmitted infection with hepatitis C virus.[2]

Donations from new donors contributed 12% of the total number of donations collected in England during 1993-5. Seroconversion rates in new donors cannot be directly measured, and there are reasons to expect that recent infections in new donors may be more frequent than in repeat donors; repeat donors have been tested for negativity for markers of infection with hepatitis C virus, hepatitis B virus, HIV, and *Treponema pallidum*, and new donors may be more likely to donate blood to obtain testing after having been exposed to infection.

Opportunities for further work

Surveillance of donation testing and of donors who seroconvert for hepatitis C virus between donations continues to be an important component of monitoring the safety of the blood supply. Study of possible exposures to infection that are associated with seroconversion for hepatitis C virus and of the course of infection in seroconverting blood donors who have a known date of infection should further contribute to our understanding of the epidemiology and clinical course of hepatitis C.

We thank Mr Mike Brittain and Trent blood centre for data on the interval between blood donations, Dr Paddy Farrington for statistical help, and all the staff of the blood centres and public health laboratories in England who provided data and responded to requests for supplementary information about testing for hepatitis C virus.

Contributors: JAJB initiated the survey, reviewed the test results and evidence for seroconversion for each reported case, contributed to the interpretation of the data and to writing the paper, and is guarantor for the paper. KS coordinated the survey, collated the data, conducted the analyses, and contributed to the interpretation of the data and to writing the paper. JH discussed core ideas and contributed to the interpretation and presentation of the data and to writing the paper.

Funding: The study was conducted by staff employed by the Public Health Laboratory Service and the National Blood Service.

Conflict of interest: None.

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(Accepted 4 February 1998)

Hematology, 1998, Vol. 3, pp. 333–338
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Transfusion

Estimation of the Infectious Risks of Blood Transfusion

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(Received 20 July 1998; In final form 26 August 1998)

Despite the success of efforts made to prevent the transmission of infections by blood transfusion, the risk of infectious donations entering the blood supply and transmitting infection to the recipients of blood components and blood products remains a concern. Following the implementation of donor selection and donation testing strategies to exclude HBV, HIV, and HCV infectious donations from the blood supply, direct observation of transmission of these viruses by blood transfusion has become rare and indirect estimation of the probable frequency of infectious donations entering the blood supply has become more common. Published estimates for different blood services and different periods of time have varied in their methods and scope. The limitations of the estimation process should be considered when using estimates of the risk of infectious donations entering the blood supply to address questions about blood safety.

Keywords: Blood transfusion, HIV, HCV, HBV, transmission, estimated risk

INTRODUCTION

Transfusion of blood collected from one individual into another carries with it the possibility of transmitting diseases caused by blood-borne infectious agents. This is particularly important as patients receiving blood transfusions are often immunosuppressed or otherwise relatively vulnerable to infection. Transmission of syphilis (*Treponema pallidum*) was recognised in the early days of transfusion when blood was transferred directly from donor to recipient. Testing donations for treponemal antibodies and storage of blood between collection and transfusion has overcome this problem. Since then, three viral infections-HBV, HCV, and HIV-have been the predominant transfusion-transmitted agents to cause disease and to prompt changes in transfusion practice. The use of factors associated with these blood-borne infections to exclude individuals from donating blood, and the testing of blood donations for markers of these infections have greatly reduced the risk of infectious donations entering the blood supply. Nevertheless, some risk will always remain because donor selection and serological testing of dona-

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tions can not identify and exclude every infectious donation. As the risks of transmitting these infections by transfusion have decreased it has become increasing difficult to directly measure, or quantify, these risks and more attention has turned to theoretical estimation of the risks of infections being transmitted by transfusion.

RISK ESTIMATION

Table I shows some key items of information required to calculate theoretical estimates of the risk of a donation infectious for a given organism entering the blood supply. The range of values in which each of the variables in Table I might lie depends on the sample used to estimate the variable, the biological variability involved, and the assumptions made in obtaining the working value. Table II summarises some published studies that have provided theoretical estimates of the risk of transfusion–transmitted infections. All of these studies have attempted to estimate the risk of window period donations (*i.e.*, i. in Tab. I) associated with donations from repeat donors. Some studies have included estimation of the risk of false negative results and errors (*i.e.*, ii. in Tab. I). In all, the risk of persistent (or fluctuating) seronegativity during established infections (*i.e.*, iii. in Tab. I) in blood donors has not been included or has been assumed to be zero.

In the USA the fall in the estimated risk of accepting HIV infectious donations between 1987 and the early 1990s was largely due to a reduction in the length of the window period used in the risk calculations (from 56 days to 22 days). The markedly higher estimated risk of HIV infectious donations in the Thai study is largely the result of the higher incidence of HIV infection in Thailand than in Europe and North America, although the longer window period used in this study also contributed to this higher estimated risk. The published studies have varied in whether they have estimated the risk from all donations, or just from donations from repeat donors. New (*i.e.*, first time) donors differ from repeat donors in ways that affect the risk of an infectious donation entering the blood supply. Probably most important is that new donors have not been previously tested by the blood service for markers of infections used to exclude individuals from the donor panel. So, donations from new donors have a higher prevalence of infectious markers. Incidence of infection can be derived from donation testing in two ways; by testing donations for markers indicative of an early infection (*e.g.*, IgM class of antibody to

TABLE I Key information for estimating the risk of donations infectious for known pathogens entering the blood supply despite donation testing

Component of risk	Information needed and source of that information	
	Derived from donation testing	Other sources
i. risk of seronegative infectious donation being collected during early infection	• Incidence of infection in donors	• Length of the infectious seronegative window period following infection
ii. risk of seropositive donation entering the blood supply through test failure or process error	• Prevalence of marker used to indicate infectivity in donations	• Sensitivity of tests for the marker • Rate of errors that could lead to failure to identify or withdraw a positive donation
iii. risk of seeronegative infectious donation being collected from donors with established (not early) infection		• Frequency of seronegative, infectious individuals (other than those in the window period following infection) amongst blood donors

TABLE II Published risk estimation studies

Country (Year of data/ estimates)	Estimated risk infectious donations per million donations (range*)	Window period (WP) risk estimated?	Length of infectious window period used in days (range)	False negative(FN) and error risk estimated?	Test sensitivity (S) and error rate (ER) used	Estimates for new donor donations included?
USA [8] (1986–87)	HIV 26	Yes	56 (28–98)	Yes No	S: 99% –	Partially WP = No FN = Yes
USA [9] (1987)	HIV 6.5 (3.33–11.33)	Yes	56	No Yes	– ER: 0.1%	Yes
USA [10] (1987)	HIV 4.64	Yes	56	No No	– –	Yes
UK [11] (1986–87)	HIV:1986 3.2 HIV:1987 1.1	Yes	56	Yes No	S: 98% –	Partially WP = No FN = Yes
Australia [12] (1985–90)	HIV 1.08	Yes	28–42	Yes No	S: 99.69% –	Yes
USA [13] (1991–93)	HIV 2.03 (0.36–4.95) HTLV 1.56 (0.50–3.90) HCV 9.70 (3.47–36.11) HBsAg 6.65 (2.87–13.43) HBV 15.83 (6.82–31.97)	Yes	22 (6–38) 51 (36–72) 82 (54–192) 59 (37–87)	No No	– –	No
USA [14] (1992–93)	HIV 1.52–2.22	Yes	average of 25	No Yes	– ER: 0.5%	Yes
France [15] (1992–94)	HIV 1.75 (0.3–4.6) HTLV 0.17 (0.0–1.6) HCV 4.48 (1.7–10.0) HBsAg 3.13 (0.9–11.2) HBV 8.45 (2.8–25.2)	Yes	22 (6–38) 56 (24–128) 66 (38–94) 51 (36–72)	No No	– –	No
Australia [16] (1994–95)	HIV 0.79 (0.22–1.37) HCV 4.27 (2.82–10.01) HBsAg 2.71 (1.70–4.00) HBV 6.45 (4.05–9.52)	Yes	22 (6–38) 82 (54–192) 59 (37–87)	No No	– –	No
Thailand [17] (1990–93)	HIV:1990 380 (210–650) HIV:1991 190 (100–340) HIV:1992 200 (110–360) HIV:1993 190 (50–670)	Yes	45	No No	– –	No

* Various methods.

hepatitis B core antigen, p24 HIV antigen, nucleic acids, or testing for low titre anti-HIV with recently proposed de-tuned antibody assays), or by using seroconversions in repeat donors that mark infections that have arisen since a previous donation. The former approach was not used in any of the studies listed in Table II. All except one used the latter approach. Brookmeyer *et al.*, did not use donation testing data at all but utilised back-calculated estimates of the infection curve in the United States. Unfortunately seroconversions can only be observed in repeat donors: additional information and assumptions have to be used to obtain an estimate of incidence in new donors. Cumming *et al.*, used the prevalence observed in donations and assumptions about the time donors had been at risk of HIV infection to estimate incidence rates in donors tested for the first time. Lackritz *et al.*, used the prevalence observed in donations from new and from repeat donors during the first year of testing and assumptions about how the difference between these prevalences represented differences in incidence. Dax *et al.*, used the prevalence observed in donations and assumptions about

the time course of HIV infection and about the probability of donating throughout that time.

Studies frequently state that the risk of a donation being collected during the window period is the largest remaining risk of infection transmission (for infections that donations are tested for). This is often an assumption rather than a proven fact. The relative importance of the different components of the risk of accepting infectious donations varies between blood services depending on the specifications of donation testing, the proportion of donations collected from new donors and the rates of incidence and prevalence in the donating population. For example, the greater the proportion of donations collected from new donors the larger the contribution to the overall risk is that associated with donations from new donors (the Thai study reports that 76% of all donations were collected from new donors); and the greater the prevalence of infection the more important the risk of false negative tests and errors in the exclusion of seropostive donations. According to an analysis of data for England (Soldan. K, Barbara. J. *et al.*, Unpublished work), 1993–1995, less than 10% of the total estimated risk of an HCV infectious donation entering the blood supply in England would be due to window period donations from repeat donors (window period for anti-HCV of 66 days (54–192), test sensitivity for anti-HCV of 98%, error rate of 0.5%). Studies that omit some components of risk or only consider donations from repeat donors would usually underestimate the risk of an infected donation entering the blood supply.

LIMITATIONS OF RISK ESTIMATION – METHODS

In most risk estimation studies estimates of incidence based on seroconversions have been a key element. The use of seroconversions to estimate incidence involves an assumption that donors are not more likely to self-defer, either temporarily or permanently, after they have seroconverted and that the probability of an individual donating blood does not vary over the course of antibody development after infection. There are some observations such as longer than average interdonation intervals in donors who have seroconverted for antibodies to HCV [1], and fewer than expected HIV p24 antigen positive, HIV antibody negative donations in the USA [2], that suggest that donors are more likely to self-defer during the window phase. This may be due to a perception of recent risk or due to symptomatic primary infection.

HBsAg negativity during established HBV infection can occur in healthy adults at the tail-end of HBV carriage. Transmission from such donors has been observed [3] and this risk should be included in estimates of total risk where blood services use HBsAg alone as a marker of HBV infective donations.

The sensitivity of assays is typically estimated using a panel of samples considered representative of the population positive for the marker concerned. The potential of newly recognised subtypes and variants of viral infections to escape detection by assays is not addressed by most risk estimation studies. Since HIV antibody testing began, there has been an emphasis on improving the sensitivity of tests with regard to early seroconversion concentrating on the HIV sub-type that has been most common in Europe and the USA, sub-type B. Other subtypes of HIV-1 infection have become more globally distributed, and the importance of ensuring assays have high sensitivity to a comprehensive range of HIV sub-types, should not be overlooked [4]. Mutant HBV infections, not detected by HBsAg tests, have also been shown to pose a risk [5].

Data that could verify of refute the results of risk estimation studies are rare. The introduction of nucleic acid testing of donations should detect infectious donations missed by current serological tests and therefore provide some data to

compare with the estimates. However, if the estimates from Europe and the USA are close to, or higher than, the true risk, several years of data collection from nucleic acid testing will be needed to test the accuracy of the estimates.

LIMITATIONS OF RISK ESTIMATION – USEFULNESS

The comparability of these estimates to other risks of morbidity is not straightforward. Infectious donations entering the blood supply do not directly translate to infected recipients. The actual risk of disease also depends upon the transmission rate, susceptibility of the recipient and the natural history of transfusion–transmitted infections in recipients. Information about natural history is often only available from case reports or from studies in other patient groups. The size of the infective dose, and the relatively poor health status of recipients, may make transmission (and rapid disease progression) more likely. On the other hand, some infectious agents may loose viability during their storage between collection and transfusion.

The communication and use of risk estimates is often difficult [6]. Misunderstanding of these risk estimates, or ignorance of their limitations can lead to a false sense of confidence, or a false sense of alarm, in the safety of transfusion.

Only those components of risk that we know about are estimated and the accuracy of the estimates is only as good as the accuracy of the information used to derive them. While these estimates of the risk of infectious donations being accepted and entering the blood supply can be of value, they can give the misleading impression that the true and total infectious risk of transfusion is known. They should not be allowed to detract attention and resources away from unestimated risks. The true infectious risks of blood transfusion involve both infections already and demonstrably blood-borne (such as HBV, HIV and HCV), and those that have not yet been identified. The latter category may have considerable impact on blood services [7] and represents a potential hazard of transfusion that has been repeatedly realised as blood-borne infections have been recognised. These as yet unidentified risks justify the use of generic measures to limit the exposure of recipients such as restricting donation pooling, the use of viral inactivation and the avoidance of unnecessary transfusion therapy.

Acknowledgment

We thank Janet Mortimer and Mary Ramsay for comments on drafts of this article.

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Reprinted from the **BMJ**, *9 January 1999, Vol 318, p 95*

Acute hepatitis B infection associated with blood transfusion in England and Wales, 1991-7: review of database

K Soldan, M Ramsay, M Collins

Blood donations in England and Wales are collected from healthy donors who do not acknowledge factors associated with an increased risk of bloodborne infections. All donations issued for transfusion since the early 1970s have been tested for hepatitis B surface antigen as a marker of transmissible hepatitis B virus. These measures have resulted in low rates of transmission by transfusion but have not eliminated all infectious donations from the blood supply.

Hepatitis B infections in transfusion recipients are investigated by the national blood services to identify if they were transmitted by transfusion. A donation is concluded as having been probably infectious if the donor was surface antigen negative but had evidence of acute infection or of carrying the virus (antibody to hepatitis B core antigen with no or low titres of antibody to surface antigen[1]) or if the donor was surface antigen positive (on review of test results or retesting archived serum) and blood was erroneously released. Mutant strains of hepatitis B virus not detected by routine surface antigen tests also pose a risk of infectious donations being transfused.[2]

Acute hepatitis B infections, and the probable route of infection, are reported voluntarily by laboratories in England and Wales to the Communicable Disease Surveillance Centre. We examined these reports to describe the frequency and nature of acute hepatitis B infection transmitted by transfusion.

Methods and results

We reviewed cases of acute hepatitis B infection reported to the surveillance centre during 1991-7 and sought information from the national blood services for cases associated with transfusion (table). Twenty four of 4185 (0.6%) cases were associated with transfusion in England and Wales. For 10 reports investigation by the national blood services was not possible (for example, donation identifiers not available) or inconclusive (for example, one or more donor not traced for retesting), or information was not available retrospectively. Of the 14 probably infectious donations that were identified, three were from surface antigen negative donors during acute hepatitis B infection and 11 were collected from negative donors during late carriage of the virus. No reports of erroneous release of surface antigen positive blood were identified.

Comment

Over 2.5 million donations are issued annually in England and Wales. The cases presented here underestimate the number of hepatitis B infections transmitted by transfusion as infection is often asymptomatic and not all acute infections are diagnosed and reported. Nevertheless, these data show that transmission of hepatitis B by transfusion does occur but is rare in England and Wales. Transfusion accounts for only a small part of the total burden of acute symptomatic hepatitis B infection and most cases are due to carriage of infection rather than acute infections in donors. A similar observation was made by the North London Blood Centre during 1985-93 (John Barbara, personal communication).

Donor selection criteria aim to exclude people with recent risk factors for acquiring bloodborne infection. Persistent hepatitis B infections often follow perinatal or childhood infection and therefore are less likely to be excluded by donor selection. Testing for antibodies to hepatitis B core antigen, as is routine in some other countries, would have detected most of the infectious donations identified. Since testing for antibodies to core antigen would also detect non-infectious donations from donors with naturally acquired immunity to hepatitis B further tests would be needed to avoid unnecessary loss of donations.

Further consideration of the costs and benefits of testing donations for antibodies to core antigen is warranted. Policies to vaccinate people who receive multiple transfusions[3] remain justified. The serious hazards of transfusion scheme[4] and collaborative work between the national blood services and Public Health Laboratory Service will continue to monitor post-transfusion infections.

We thank the laboratories and blood centres for providing the reports and follow up information necessary for this study.

Contributors: MC managed the reports of acute hepatitis B infection and extracted the data. MR initiated the study and participated in the data interpretation and writing the paper. KS coordinated the study and participated in the writing of the paper and is the study guarantor. John Barbara discussed the data with the authors and commented on the paper.

Funding: None.

Conflict of interest: None.

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(Accepted 15 September 1998)

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BMJ 1999;318:95

Reports of acute hepatitis B infection associated with transfusion, England and Wales, 1991-7*

Year	Total reports	Transfusion in UK most probable route of infection	Donor surface antigen negative: Acute infection	Donor surface antigen negative: Carrier	Investigation of donor not available or inconclusive
1991	572	5	0	2	3
1992	531	3	1	1	1
1993	629	5	1	4	0
1994	631	3	0	2	1
1995	613	5	0	1	4
1996	581	2	1	1	0
1997	628	1	0	0	1
1991-7	4185†	24 (0.57%)	3	11	10

*Data at 31 March 98. †For 21 reports the most probable route of infection was transfusion abroad (not known to have been confirmed by investigation of the implicated donations), and for three reports no information about the place of transfusion was provided.

reprovision programmes in Britain, provided that these are well planned and well resourced.

Conclusion

Our findings dispel some of the common concerns and myths associated with "care in the community" patients and provide robust evidence that community care has worked well for the former patients of psychiatric hospitals, most of whom are currently living in the community and posing minimal risk to themselves and the public. In light of this, a change towards institutional care is not a rational policy.

We thank the research workers who have contributed to the collection of the data, the patients, and the hospital and community staff. This paper is designated the TAPS project 45.

Contributors: NT participated in data collection, analysis, interpretation, and drafting the paper. JL conceived and designed the Team for the Assessment of Psychiatric Services (TAPS) project and has been the director of the research team for the past 13 years. He helped to draft and edit this paper. GG participated in the analysis and interpretation of the mortality data. He also computerised the assessment tools used by TAPS. NT and JL will act as guarantors for the paper.

Funding: The Team for the Assessment of Psychiatric Services (TAPS) is funded by the Department of Health, North Thames Regional Health Authority, and the Gatsby Foundation. It is administered through the Department of Psychiatry and Behavioural Sciences, Royal Free and University College Medical School, London.

Competing interests: The TAPS project was largely funded by the Department of Health. This, and previous TAPS papers, were sent for comments to the Department of Health before submission. However, all papers, including this one, were drafted without administrative intervention or scrutiny of any kind. The opinions expressed do not necessarily reflect the policy of the Department of Health.

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(Accepted 30 March 1999)

Serious hazards of transfusion (SHOT) initiative: analysis of the first two annual reports

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BMJ 1999;319:16–9

Abstract

Objective To receive and collate reports of death or major complications of transfusion of blood or components.
Design Haematologists were invited confidentially to report deaths and major complications after blood transfusion during October 1996 to September 1998.
Setting Hospitals in United Kingdom and Ireland.
Subjects Patients who died or experienced serious complications, as defined below, associated with transfusion of red cells, platelets, fresh frozen plasma, or cryoprecipitate.
Main outcome measures Death, "wrong" blood transfused to patient, acute and delayed transfusion reactions, transfusion related acute lung injury, transfusion associated graft versus host disease, post-transfusion purpura, and infection transmitted by transfusion. Circumstances relating to these cases and relative frequency of complications.
Results Over 24 months, 366 cases were reported, of which 191 (52%) were "wrong blood to patient" episodes. Analysis of these revealed multiple errors of identification, often beginning when blood was collected from the blood bank. There were 22 deaths from all causes, including three from ABO incompatibility. There were 12 infections: four bacterial (one fatal), seven viral, and one fatal case of malaria. During the second 12 months, 164/424 hospitals (39%) submitted a "nil to report" return.
Conclusions Transfusion is now extremely safe, but vigilance is needed to ensure correct identification of blood and patient. Staff education should include awareness of ABO incompatibility and bacterial contamination as causes of life threatening reactions to blood.

Introduction

The current incidence of major complications due to blood transfusion is unknown. Until 1996 blood transfusion was not covered by either a confidential inquiry or the yellow card system of the Committee of Safety of Medicines. Perception of transfusion safety focuses on the diminishing risk of viral transmission, while the risk of ABO incompatible transfusion due to errors in blood or patient identification remains a threat.[1,2] To analyse the residual risks of transfusion, a confidential voluntary reporting system for major transfusion events—serious hazards of transfusion (SHOT)—

Morbidity and mortality related to transfusions in fully analysed cases (n=341)

Detail	Total	Incorrect component transfused	Major acute transfusion reaction	Major delayed transfusion reaction	Post-transfusion purpura	Graft versus host disease	Transfusion related acute lung injury	Transfusion transmitted infections
Death attributed to transfusion	22	3	1	3	1	8	4	2
Major morbidity*	84	32†	2	16	5	0	19	10
Minor/no morbidity	235	141	47	31	16	0	0	0
Total	341	176	50	50	22	8	23	12

*Admission to intensive care or ventilation, or both; dialysis or renal dysfunction, or both; major haemorrhage; jaundice including intravascular haemolysis; persistent viral infection; acute symptomatic confirmed infection.
†Includes six cases of potential rhesus sensitisation in young women/girls.

affiliated to the Royal College of Pathologists was launched in 1996. We have summarised the main findings from its first two annual reports.

Methods for case ascertainment

In November 1996 haematologists in the United Kingdom and Ireland were invited on a voluntary confidential basis to inform SHOT of deaths and major adverse events in seven categories (see results) associated with the transfusion of red cells, platelets, fresh frozen plasma, or cryoprecipitate. The SHOT launch was publicised at professional conferences and by an editorial in the *BMJ*.[3] Suspected cases of post-transfusion infection were reported to local blood centres, and cases confirmed after donor investigation as related to transfusion were collated by the National Blood Authority/Public Health Laboratory Service Communicable Disease Surveillance Centre.

Incidents other than infections reported to the SHOT office were analysed with a questionnaire then entered on a secure database without identifiers. During the second year hospitals could submit a "nil to report" return card. We have analysed data relating to incidents that occurred between 1 October 1996 and 30 September 1998.

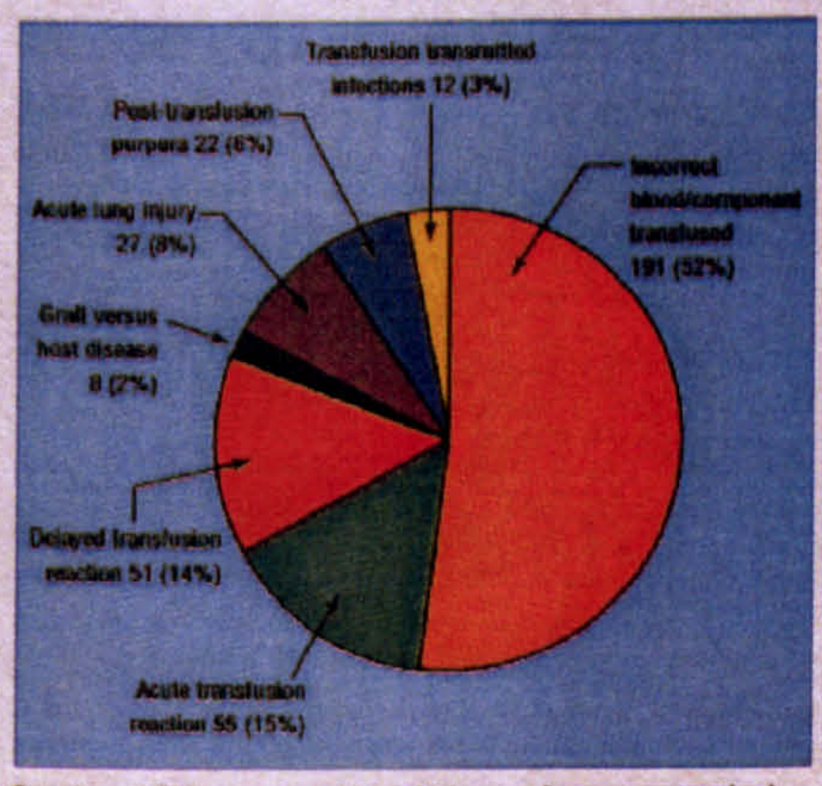
Results

Overview

Of 424 eligible hospitals, 94 submitted 169 reports during the first year, with 112 hospitals submitting 197 reports during the second year, an increase of 16.5%. "Nil to report" cards, introduced in the second year, were submitted by 164 hospitals (39%), bringing overall participation to 65%. Reports included 191 incidents of incorrect blood transfused and 12 infections transmitted by transfusion (figure). Of 341 analysed cases, there were 22 deaths and 81 cases of major morbidity, with at least one death in every category (table).

Incorrect blood or component transfused

Of the 191 reported episodes in which a patient was transfused with a wrong blood component, 62 were ABO incompatible transfusions, leading to three deaths, 25 cases requiring intensive care, and six cases of potential rhesus D sensitisation in young female patients. The errors in 177 analysed cases of incorrect transfusion generally consisted of a sequence of one to seven failures to detect incorrect identity of blood or patient, leading to transfusion to the wrong patient (one error—103 cases; two errors—40 cases; three errors—26 cases; four errors—2 cases; six errors—5 cases; seven errors—1 case). First errors occurred at all stages of the process: during the request for blood or sampling of the patient, or both (33), including two incidents (one fatal) of transposition of blood grouping samples at the patient's bedside, and in the transfusion laboratory (59). Collection of the wrong blood from the blood bank refrigerator was the major source of primary error (61), with blood frequently taken without a formal identity check against the patient's case record. The bedside check failed to detect discrepancy in blood or patient identity in a total of 80 cases, despite being carried out by two people (one always a qualified nurse or doctor). In 20 incidents, the patient had no identity wrist band.



Overview of 366 cases for which initial report forms were received

Immunological interactions between donor and patient

Immunological interactions were reported in five categories (acute and delayed reactions, post-transfusion purpura, transfusion associated graft versus host disease, and transfusion related acute lung injury). These cases were unpredictable and generally did not represent poor practice. In two cases, however, haemolytic antibodies were missed because of non-compliance with current guidelines.[4] Occasionally, relevant information was not available because the blood bank computer could not be accessed.

Five reports were received of a hypotensive reaction to components passed through a bedside leucocyte filter.[5] Of eight cases of transfusion associated graft versus host disease, one was a premature neonate with an unusual form of immunodeficiency and four patients had B cell lymphoid malignancy, not currently an indication for prevention of transfusion associated

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Summary of main findings and recommendations

Finding	Recommendation
Prelabelled cross match sample tubes are a source of misidentity	Current BCSH guideline recommends labelling at the bedside after the sample is drawn
Request for blood may omit special requirements, especially over the telephone	Request systems must ensure that all requirements are met and that responsibilities of ward and blood bank staff are clear
Previous transfusion information was not always used in decision making	Previous transfusion records should be available at all times and blood groups checked with current results
Blood bank errors in grouping, cross matching, and labelling were found	Blood banks should review procedures for adherence to national guidelines and ensure ongoing staff training
The most important primary cause of error was in collecting blood from the blood bank	Hospitals should review current procedures and define minimum identification requirements. Novel IT systems merit evaluation
Lack of patient wristbands or other identifiers was a source of wrong blood being transfused	Procedures to ensure correct patient identification are particularly important in theatre and for outpatient transfusions
Earlier errors are not being detected at the final bedside check, even if two qualified staff check the blood	BCSH will produce a national guideline to cover this issue; hospitals will be responsible for implementation and staff training
Local systems for staff training and oversight of transfusion practice are variable	Every hospital should have a transfusion committee with responsibility for all matters related to transfusions
Several organisations are responsible for decision making in transfusion safety	A unified approach to setting priorities for transfusion safety would ensure best use of resources
Investigation of transfusion reactions was variable and may have led to underestimation of bacterial transmission	Standardised protocols for joint investigation of suspected bacterial sepsis and immunological reactions between hospitals and blood centres would be helpful

graft versus host disease by the use of γ irradiated blood components.

Transfusion transmitted infection

Twelve of 60 suspected cases (20%) were confirmed to be related to the transfusion. Six cases (one hepatitis A infection, one malaria, four bacteraemias) were due to infections for which no testing of donations is performed, while five cases (three hepatitis B, one hepatitis C, one HIV) were due to donations from repeat donors during marker negative "window periods" after recent infection. A further newly reported case of infection with hepatitis C virus was in a patient who received a transfusion before the introduction of donor screening in 1991. The HIV transmission involved components from one donor transfused to three different recipients. The three non-fatal bacterial incidents involved red cells contaminated with *Serratia liquefaciens*, platelets containing *Escherichia coli*, and leucocyte depleted platelets containing *Bacillus cereus*, also grown from the donor's arm. Fatal septicaemia due to *Staphylococcus aureus* occurred in one platelet recipient. *S aureus* was also isolated from the donor's skin and nose.

The other fatality caused by infection was due to cerebral malaria after transmission of *Plasmodium falciparum* from a donor who lived in a malarious area as a child and who had revisited a (different) malarious area within the previous 4 years. This has already led to amendments to selection criteria for donors.

Key recommendations and feedback

Major findings and the recommendations arising from them are summarised in the box. Detailed annual reports were sent to all haematologists,[6,7] with a summary to trusts' chief executives and blood bank managers. Seventy nine hospitals had already reviewed procedures for blood handling and staff training after the incident reported. The SHOT findings were highlighted at a transfusion seminar organised by the United Kingdom chief medical officers, and participation in SHOT was recommended in a health service circular to trusts.[8]

Discussion

Voluntary reporting of serious complications of transfusion has its limitations—we may be seeing only the tip of the iceberg, viral infections may present years after acquisition, and there are no denominators from which to calculate hazard incidence. The incidence of ABO incompatible transfusions reported here (62 in 2 years), however, is not significantly different from that seen in the French haemovigilance system (58 in 3 years), to which reporting is mandatory.[9] In the second year, SHOT implemented a nil to report card; this revealed that the 65% of participating hospitals handled 70% of all red cells issued in the United Kingdom. SHOT findings therefore do seem representative of transfusion practice.

Key messages

- Blood transfusion, while extremely safe, has several potentially fatal hazards
- All staff handling blood should be aware of the importance of correct identity of sample, patient, and blood bag at all stages
- Resources should be directed to evaluation of methods for improving identification of patients
- Acute fever or collapse during or after transfusion may be due to ABO incompatibility or bacterial contamination
- Microbiological complications of transfusion accounted for a minor component of all reports

The two annual reports have provided the first detailed analysis of transfusion errors in the United Kingdom, an approach already recommended in the United States.[10] Following defined procedures for blood handling[11] and regular staff training are crucial; bedside ABO grouping has a high error rate[12] and is not recommended by SHOT, although it is mandated in France. Medical and nursing staff must be aware of the possibility of ABO incompatibility or bacterial infection in a shocked recipient of transfusion, while errors in identification will be minimised by procedural training for porters and phlebotomists and by forthcoming guidelines for blood handling and administration from the British Committee for Standards in Haematology. Infections transmitted by transfusion were relatively rare, a finding consistent with the calculated low residual viral risk,[13] now overtaken by the frequency of bacterial contamination of platelet concentrates.[14] SHOT data provide mixed messages: the risk:benefit ratio of appropriate transfusion is high compared with other risks in life,[15] but safety can still be improved. The United Kingdom lacks a unified body to take an overview of all aspects of blood safety, sometimes making it difficult to practise "aligning effort with risks."[16] Technological advances such as viral genomic detection and inactivation may be mandated by regulatory authorities, but prevention of transfusion error requires local managerial commitment, "process re-engineering,"[17] and an active hospital transfusion committee. Hopefully the concept of clinical governance will focus resources in this important area.

Contributors: LMW, EML, PS, and JAJB took part in the establishment of the SHOT scheme, design of the questionnaire, analysis of data, and compilation of the report. SL, HC, and KS took part in design of the questionnaire, analysis of data, and compilation of the report. DBLMcC took part in the establishment of the SHOT scheme, analysis of data, and compilation of the report. LMW, HC, and EML are the guarantors.

Funding: UK Transfusion Services, Republic of Ireland Transfusion Service, British Society for Haematology, British Transfusion Society.

Competing interests: None declared.

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(Accepted 19 April 1999)

Cost minimisation analysis of provision of oxygen at home: are the *Drug Tariff* guidelines cost effective?

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Abstract

Objectives To determine the level of oxygen cylinder use at which it becomes more cost effective to provide oxygen by concentrator at home in Northern Ireland, and to examine potential cost savings if cylinder use above this level had been replaced by concentrator in 1996.

Design Cost minimisation analysis.

Setting Area health boards in Northern Ireland.

Main outcome measures Cost effective cut off point for switch to provision of oxygen from cylinder to concentrator. Potential maximum and minimum savings in Northern Ireland (sensitivity analysis) owing to switch to more cost effective strategy on the basis of provision of cylinders in 1996.

Results In Northern Ireland it is currently cost effective to provide oxygen by concentrator when the patient is using three or more cylinders per month independent of the duration of the prescription. More widespread use of concentrators at this level of provision is likely to lead to a cost saving.

Conclusions The *Drug Tariff* prescribing guidelines, advocating that provision of oxygen by concentrator becomes cheaper when 21 cylinders are being used per month—are currently inaccurate in Northern Ireland. Regional health authorities should review their current arrangements for provision of oxygen at home and perform a cost analysis to determine at what level it becomes more cost effective to provide oxygen by concentrator.

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BMJ 1999;319:19–23

Introduction

In the United Kingdom, the provision of oxygen at home can be prescribed either in cylinders (capacity of

Reprinted from JOURNAL OF CLINICAL PATHOLOGY, June 1999, Vol 52, No 6, p 405-408

Leader

The risks of infection transmission by blood transfusion in England

Kate Soldan, John Barbara

Strategies implemented to prevent transmission of infections by blood transfusion have been very successful. Despite this, the risk of infectious donations entering the blood supply and transmitting infection to the recipients of blood components and blood products is continually under scrutiny.

In order to assess the risks and consequences of transfusion transmitted infections the characteristics of blood borne infections, of donations, and of blood recipients need to be considered. Over the years, knowledge about new agents and about potential failures in the strategies to exclude known agents has increased. Consequently the range of possible strategies to exclude infections from the blood supply has also increased, and debate about the risks of infection transmission by blood transfusion has become more complex.

Transfusion transmissible infections

At certain stages in their natural history many viral, bacterial, and protozoal infections can be blood borne and may be transmitted by transfusion. Fortunately for transfusion medicine, many blood borne organisms cause symptoms that render their victims too unwell, or obviously unfit, to donate blood. Other agents are only present in the blood transiently and some agents do not survive the conditions of blood storage outside the human body.

Variations in the length of time over which agents are present in the blood, and are viable in stored blood, determine to a large extent the variations in the risk that infectious donations will be collected. Infections of most concern are those that have long periods of infectivity in the absence of any clinical signs or symptoms of infection and are stable in stored blood (for example, hepatitis B virus (HBV), HIV, and hepatitis C virus (HCV)). The length of time between infection and the development of detectable serological markers (the window period) also varies between agents (for example, 22 days for anti-HIV[1] and 66 days for anti-HCV[2] using current assays). The shorter the window period, relative to the total asymptomatic seropositive infective period, the better is the detection of infectious donations by serological testing (all other things being equal).

For infections with transient blood borne infectivity (for example, hepatitis A virus (HAV) and parvovirus B19), the risk of infectious donations being collected depends upon the incidence of the infection in the donor population and the length of the infectious period.

Strategies to reduce risk

There are three main strategies for preventing infectious donations from entering the blood supply issued to hospitals. The first concerns the recruitment and selection of blood donors who do not have a known increased risk of infection. The second is the testing of donations for serological markers of infections. The third covers the control of cleanliness during component production.

Donor recruitment and selection aims to select a group of individuals with a low risk of infection: the prevalence of infection and the incidence of infection should both be low. In practice incidence is often difficult to measure. The selection of a "low risk" group therefore often depends on identifying groups with low seroprevalence and without the characteristics or exposures associated with an increased risk of infection. There are some general guidelines for donor selection (which are well founded in experience). Voluntary donors are considered safer than paid donors, and repeat donors safer than new donors. However, selection of these individuals is not guaranteed to be effective—particularly for new infections or for infections with changing epidemiology.

New knowledge about exposures of increased risk for blood borne infections is regularly considered so that guidelines for predonation donor selection in the United Kingdom can be revised as necessary. Inapparent infections and non-recognition or denial of risk factors in donors prevents the exclusion of all infected donations by predonation selection criteria.

Over the years there has been a steady introduction of available measures to reduce risks that have been recognised. Table 1 shows the tests for markers of transfusion transmissible infection that are currently performed on all blood donations in the United Kingdom. The introduction of each of these tests has led to a reduction in the number of transfusion transmitted infections (table 1). During the first full year of anti-HIV (1986) and anti-HCV (1992) testing in England and Wales, 38 and 807

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Accepted for publication
9 November 1998

Table 1 Routine testing for markers of transfusion transmissible infection in England and Wales and the effect of testing on the prevention of infections in blood transfusion recipients

Assay	*Date of introduction to routine donation testing*	*Number of positive donations excluded by testing during 1997*	*Reduction in transfusion transmitted infections in England and Wales following introduction of routine test**
Treponemal antibodies	By 1950	100 (1 in 26 703 donations)	Uncertain: it is difficult to ascribe reduction in transfusion transmitted syphilis to testing since storage at 4 C leads to inactivation of *T pallidum*
HBsAg	Early 1970s	123 (1 in 21 710 donations)	There was a marked fall in post-transfusion acute HBV infections: eg, North London blood centre recorded 30 reports of cases in 1970, 12 in 1972, 6 in 1974, and 3 in 1976[1]
Anti-HIV 1	October 1985	29	69 HIV infections were diagnosed that were probably transmitted by transfusion in the UK before 10/85†, and 3 that were transfused between 10/85 and the end of 1997.
Anti-HIV 1 and 2	June 1990	(1 in 92 079 donations)	
Anti-HCV	September 1991	236 (1 in 11 315 donations)	Transfusion before 9 91 has been associated with 128 laboratory reports (4.3%) of HCV infection with risk factor information (1992–1996).[4] Between 1/10/95 and 30/6/98, one case of HCV transmission by transfusion post 9 91 has been reported‡

*Other factors, such as improved donor selection, will have contributed.
†Source: PHLS AIDS Centre (data as of 1 September 1998).
‡Source: NBA/PHLS CDSC, unpublished infection surveillance report No 7.
HbsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

positive donors were identified, respectively—thus preventing the donations from these donors entering the blood supply. As time passes following the introduction of a marker test, and the population of repeat blood donors passes through the testing process, the overall rate of infectious donations identified decreases. The number of positive donations excluded from the blood supply in England and Wales by donation testing during 1997 is shown in table 1. Many, if not all, donations positive for HBsAg, anti-HIV, or anti-HCV are expected to lead to infection in at least one blood recipient if they are not excluded from the blood supply.

Maximising the effectiveness of donation testing includes assuring good test performance. This can be obtained by the evaluation of test kits, and test kit batches, for suitability and reliability in the blood centre setting, before their use by transfusion services. Monitoring performance once a test is in use is also important.

Testing blood donations improves the safety of the blood supply in two direct ways:

- Infectious donations found to be positive for markers of infection at the time of donation are removed.
- Infected donors are excluded from the donor population, and infected donations are therefore prevented from entering blood centres in the future.

These factors can be quantified to assess the benefits of donation testing.

Testing also improves the safety of the blood supply in two indirect ways:

- Donors who are at increased risk of blood borne infections are excluded from the donor population. As blood borne infections often have common routes of transmission, donors with evidence of one infection may be at increased risk of having other blood borne infections that are not detected by donation testing. Also, some individuals who have been in contact with infected donors (for example, sexual contacts) may be at increased risk of infection, and infected donations may be prevented from entering blood centres if these individuals are instructed not to donate blood.
- The diagnosis of infection in a donor, and the surveillance of infections and risk factors in donors, can improve methods of donor selection—for example, the detection of HCV antibodies in blood donors revealed a large group of donors who had been exposed to blood borne infections by injecting drugs.[5]

The probability of transmitting an infection by blood transfusion can be reduced by certain manufacturing processes and conditions. Strict control of cleanliness during component production limits the opportunities for bacterial contamination. Storage of whole blood and red cells at 4±2°C limits the growth of any bacteria that are present.

Developments to testing systems, and controls on those systems, that ensure the release only of negative components have been crucial in the improved safety gained by donation testing. Automation of testing, along with inclusion of controlled steps in commercial tests, has enabled strict standardisation and close monitoring of the testing process. One example of an important addition to the testing processes is sample addition monitors that change colour (measurable on a spectrophotometer) when serum or plasma is added. Another is process control automation. Use of appropriate quality control samples, as well as the manufacturer's controls and "go-no-go" samples, adds a further check on test performance. The computerisation of test results and of component release has helped to increase safety in the face of increasing numbers of donations and the increasing volume of data generated during the testing of each donation.

Practices beyond the transfusion centre also contribute to the prevention of transfusion transmitted disease. Strategies to avoid transfusion as a treatment unless absolutely necessary, and to inactivate viruses by heat or solvent detergent treatments of products, prevent exposures. Strategies to provide prophylactic

treatment to recipients can also play a useful role. For example, HBV immunisation is currently recommended for haemophiliacs, those receiving regular blood transfusions or blood products, or those carers responsible for the administration of such products.[6]

Manufacturing processes that involve pooling donations or components, for example for treatment with solvent detergents, require careful consideration. Pooling (unless the infection is neutralised by antibodies also present in the pool) can lead to a single infectious donation entering multiple products, and is therefore avoided. Pooling is particularly dangerous with regard to agents that are not excluded by testing, including agents that are as yet unknown.

Additional serological tests are performed in some countries. Some detect infections missed by current testing—for example, HIV p24 antigen and anti-HBc. Others detect transfusion transmissible infections that are currently not tested for in the United Kingdom—for example, anti-HTLV. Others detect surrogate markers of infection—for example, alanine transaminase for hepatitis viruses, low pH haemagglutination for parvovirus B19, and alpha-neopterin for detecting inflammation. The frequency of infections, and therefore the risk of transmissible infection, in donations in England and Wales has tended to be lower than in countries where additional tests have been adopted. However, this in not always the case. Factors such as the expected risk of disease occurring in recipients, the amount of public concern about blood safety and the infection in question, and the availability of resources have also played a part in determining the differences in blood testing strategies in different countries. The availability of tests for nucleic acids provides an opportunity to detect infections that cannot be detected by serological tests. Donations collected during the window period of early infection are the main candidates. Nucleic acid testing (NAT) should detect infectious donations from seronegative donors and from any seropositive donors that routine serological testing fails to detect. Nucleic acid tests are soon to be used for HCV RNA in mini-pools of plasma samples destined for pooled product manufacture.[7] The potential additional benefit for a blood service of such procedures for specific agents will depend on the epidemiology of the agent in their population.

Assessing the value of additional donation testing strategies must consider some or all of the following costs:

- the cost of test kits and reagents and related laboratory costs including staff time;
- the costs of confirmatory testing on reactive donations;
- the costs of notifying, counselling, and referring donors who are positive to new tests, or who have persistent false reactivity to the new tests used;
- the costs of replacing donors excluded because of positivity (or false persistent reactivity) to the tests used;
- the costs of any delay in the release of blood components while testing is performed;
- the costs of added data management and added complexity to the blood release procedure;
- the costs of look-backs—that is, of tracing and testing recipients who may have been exposed to infection by other donations from donors found to be positive.

Quantification of risks

Quantifying the risk of transfusion transmission of infection can be attempted by several methods, each with different limitations (table 2).

Surveillance systems monitor diagnosed transfusion transmitted infections. Several factors common to transfusion transmitted infections, and to transfusion recipients, are likely to contribute to a lack of clinically apparent symptoms and therefore to underdiagnosis of infections. Other treatments may negate or modify symptoms—many transfusion recipients are receiving antibiotic drugs and are therefore less likely to suffer observable consequences from bacterial infections. Transfusion recipients are sick or injured, and often elderly, and have high mortality from other causes. The recipients who receive relatively large numbers of transfusions, and are therefore at the highest risk of transfusion transmitted infections, have the highest mortality rates. Long presymptomatic periods are common for persistent blood borne viruses. Whether infection with a larger viral dose, at an older age, and in already ill or immunocompromised individuals alters this period is not always known. Transfusion in the past may be overlooked as a possible route of infection when diagnosis is delayed for such long periods. Naturally acquired immunity to infection may be quite high for some infections, and asymptomatic infection is common in the young age groups with low levels of naturally acquired immunity (for example, HAV and B19). Recognised cases of transfusion transmitted infections are likely to be those with the more apparent, and more severe, clinical consequences.

These ascertainment biases and limitations can be overcome by actively following up transfused recipients and testing them for evidence of transfusion transmitted infections. In the United Kingdom, transfusion transmission of infection with observed clinical consequences is rare—both in absolute terms and relative to incidents of infection transmission by other routes. The number of recipients that need to be followed up in order to obtain a precise estimate of transmission rates is therefore very large, and such studies have become prohibitively expensive. A recent study of 21 800 units found no transfusion transmitted HIV, HBV, HCV, or HTLV (human T cell leukaemia virus) I and II infections.[8]

Another approach is to estimate the number of infectious donations that current donation testing is not expected to detect. To attempt such estimation, information is needed about infection rates in the population donating blood, about the development and persistence

Table 2 Sources of quantitative data and estimates in the United Kingdom about how many transfusion transmitted infections occur (or are reported) in one year (equivalent to per 2.5 million donations)

Infection	*Surveillance of apparent cases. [Source: SHOT reports received Oct'96-Sep'97*]*	*Prospective study of transfusion recipients. [Source: study of 21 800 donations 1996] (95% confidence intervals)*	*Estimated infectious donations released into the blood supply. [Source: unpublished study using 1993-1995 donor infection data for England] (95% confidence intervals)*
HAV	1[9]	NA	NA
HIV	1 (3 recipients infected)[10]	0 (0 to 423)	0.8 (0.3 to 2.5)
HCV	1	0 (0 to 423)	11 (9.4 to 18.3)
HBV	1	0 (0 to 423)	NA
HTLV I and II	0	0 (0 to 423)	NA
Bacteria	3	NA	NA

NA, not available.
*Source: *Serious hazards of transfusion*: Annual Report 1996-1997.
HA(B,C)V, hepatitis A(B,C) virus; HIV, human immunodeficiency virus; HTLV, human T cell leukaemia virus.

of the markers that are tested for, and about the tests and the testing system used. The probability of a donation being collected during the window period when the tests used cannot detect evidence of infection depends upon the incidence of the infection and the length of the window period. The probability of symptoms that may prevent donation occurring during this period may also need to be considered. Incidence is usually calculated using observations of acute infections in donors or observations of seroconversions in repeat donors. The probability of a false negative test result depends upon the prevalence of the marker and the sensitivity of the test. The probability of a marker positive donation being released into the blood supply owing to a failure, or error, in the testing system also depends upon the prevalence of the marker and upon the probability of a failure or error.

Infectious donations do not necessarily mean morbidity in recipients, and estimating the effect of infectious donations requires knowledge about transmission and the natural history of infections.

Transfusion transmitted infections also bear a risk of onward transmission. The major risk factors for transmission of the persistent viral infections—that is, injecting drug use and sexual contact—may be relatively rare among transfusion recipients. However, this is not always the case and other types of contact—especially those common in health care settings—pose a risk of secondary transmission.

Our limited knowledge

When considering the infectivity of blood from donors, and the natural history of infections transmitted by transfusion, knowledge obtained from observing infections transmitted by other routes may not be reliable. In particular, the progression of disease caused by some viral infections may be affected by the viral load at the time of infection. An infected blood component typically exposes a recipient to a far higher viral dose than other routes of transmission.

Whether prion disease can be transmitted by transfusion is currently uncertain.[11] Unknown infections and infections with increasing potential to cause harm to recipients owing to the changing epidemiology of the infection, or changing vulnerability of blood recipients to disease, may pose the greatest risks of infection to recipients. Avoidance of unnecessary transfusion and vigilance of blood borne infectious diseases in the general population and in blood recipients are therefore important general components of transfusion medicine.

We thank Mary Ramsay for comments on the manuscript.

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BMJ Publishing Group
BMA House, Tavistock Square, London WC1H 9JR. Tel. 0171 383 6305. Fax 0171 383 6699

Printed in Great Britain by Meridian Print Centre Ltd. Derby JCP/Jun/99

International Forum

Vox Sanguinis

Vox Sang 2000;78:59–67

Bacterial Contamination of Blood Components

C.P. Engelfriet
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From the literature and from the first results of haemovigilance in some countries in which a haemovigilance system has been in force for some time, it is evident that bacterial contamination of cell concentrates, plasma and even of autologous blood is still a serious hazard of transfusion. For example, in France, where a legal obligation to report all untoward effects of blood transfusion was implemented in 1994, bacterial contamination was the most frequent cause of transfusion-related death [1] and bacterial contamination was responsible for 10% of transfusion-associated fatalities in the period 1986–1988 in the USA [2].

There are several sources of bacterial contamination, such as bacteraemia in the donor's blood, insufficient disinfection of the donor's skin, inadequate sterilization of the blood-collecting equipment during manufacture, or inadequate handling of the donated blood or the blood products derived from it. Several measures have been proposed to try to reduce the frequency of transfusion-associated septic reactions, most of which are being actively investigated [3].

It seemed of interest to gather information on this subject in an International Forum, in particular on the frequency of septic transfusion reactions and on measures taken to reduce the risk of contamination.

In order to obtain such information, the questions listed below were sent to 16 transfusion centres. Answers were obtained from 9 of them.

Questions

(1) Have you any data on the frequency of transfusion-associated septic reactions in your country/centre and if so, could you indicate the percentage of fatalities as well as the blood product involved?

(2) Have you any data on the frequency of bacterial contamination of red cell and/or platelet concentrates as determined in vitro?

(3) Have any of the measures, to reduce the risk of bacterial contamination listed below been adopted or investigated in your country/centre?

- Improvement of donor skin preparation and/or disinfection;
- removal of the first 2 ml of blood collected;
- limitation of storage time of cell concentrates;
- pretransfusion detection of bacteria; visual inspection, endotoxin assays, microbiological staining, ribosomal assays for bacteria, polymerase chain reaction, culture techniques;
- modifications of blood processing: leucocyte depletion, disinfection of waterbath, modification of the period of storage prior to component preparation, and
- others.

Comments

Question 1. The frequency of TA septic reactions varies from none in the last several years (Finland and Vienna) to 4–6 (1 fatal case) per year in Canada (see Blajchman), 7 (2 fatalities) in 3 years in the British Isles (excluding Scotland) (see Soldan) and 3 serious cases in 1997 in the Flemish-speaking part of Belgium (see Muylle). In Cleveland, where a prospective microbiological surveillance programme has been in place for more than 7 years (platelet units only), all 4 to 5-day-old units or concentrates were tested; it was concluded from the results that a septic reaction would have occurred after the transfusion of 1/500 platelet pools. In spite of surveillance, 1 fatal septic reaction occurred. In this case, 3-day-old platelets were used, which therefore had not been tested (see Yomtovian). In the USA, as a whole, septic reactions are reported in 1/10,000 to 1/20,000 units transfused and fatal reactions in 1/6 million units (see Klein). TA septic reactions are considered to be grossly underreported. An interesting case report illustrates this important issue (see Blajchman).

Question 2. Data concerning bacterial contamination mainly concern platelets. The rate of contamination found varies considerably. A survey of the main data is given in table 1. There is clear evidence that the rate of contamination increases with storage (see Blajchman and Yomtovian).

In Finland, in a series of 28,912 units investigated during 1978–1988, both red cell and platelet concentrates, were tested. Serious contamination was found in 1 red cell concentrate and in 5 platelet units.

In the multicentre study which has been initiated in the USA, both red cell and platelet concentrates will be tested.

Question 3. Measures to reduce the risk of bacterial contamination that have been adopted are as follows: improved treatment of the skin before donation (e.g. the two-step method first using isopropyl alcohol and then tincture of iodine in Canada), prestorage leucocyte depletion-reduction of both platelet and red cell concentrates, limitation of the storage time, particularly of platelets (3-5 days), visual inspection of the concentrate before use and, in some countries, routine testing of platelet concentrates for bacterial contamination (gram stain in Cleveland, Bact Alert 240 in Oslo and Belgium). Other methods of bacterial testing are being investigated. In Spain, no data are available at present, but bacterial screening procedures will soon be introduced.

In conclusion, it is clear that there is much awareness of the danger of bacterial

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Table 1. Rate of bacterial contamination of platelet concentrates

Country/centre	Platelets	Rate of contamination per 100,000	Day of testing
Canada	random units	25	day 1
		70	day 3
Finland	random PRP units	110 (1979–1994)	
	pooled BC-derived units	110 (1991–1996)	outdated
		140 (1997–1998)	
Oslo	pooled BC-derived units	44–167	day 1
	apheresis units	0	day 1
Cleveland	random units	49.7	day 4–5
	apheresis units	41.5	day 4–5
Belgium	random single units	160	day 1
	pooled concentrates	530	day 1
British Isles	single random units	0 (of 249)	day 5–7
North London	pooled random units	700	
	apheresis units	400	
Vienna	number of units tested too small		

contamination, particularly of platelet concentrates. Measures to reduce the danger have been taken. There is evidence that particularly routine testing for bacterial contamination of platelet concentrates reduces the risk of transfusion-related septic reactions.

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Morris A. Blajchman

Question 1

There is no formal haemovigilance system currently in place in Canada; however, it is a requirement of Health Canada (the Bureau of Biologicals and Radiopharmaceuticals) to report all serious adverse effects associated with the transfusion of blood products, including those due to septic transfusion reactions. Based on these reports we have had approximately 1 death annually over the past 10 years due to transfusion-associated sepsis. These deaths were associated with the transfusion of both platelets and red cells. In addition, there were 3–5 non-fatal septic transfusion reactions annually. In my opinion, however, it is likely that serious transfusion-associated septic episodes occur more frequently than the number reported. Septic transfusion reactions (fatal and non-fatal) are grossly underreported, as many serious reactions are not being recognized as being due to contaminated blood products. An example of how such underreporting might occur is exemplified by a recent Canadian case.

The blood product recipient, a 76-year-old man with severe thrombocytopenia due to myelodysplasia, received a pool of 5 units of pre-storage-filtered leucoreduced random donor platelets as an outpatient. He was not pre-medicated and did not have any symptoms during or following the transfusion of the platelet pool. Three days later, he came into hospital having been called in by his physician, who found him to be febrile (39.6 °C). Accordingly, the patient was admitted to hospital and started on antibiotics. He went into shock approximately 8 h after admission and died from the consequences of the septic shock 3 days later. Blood cultures from this patient were positive for *Staphylococcus aureus*.

The donor of the platelet unit which very likely caused the above transfusion-associated septic reaction was a 36-year-old male who had donated blood on many previous occasions. He gave a whole blood donation 4 days prior to the recipient receiving the pool of platelets which included this donor's platelet unit. Three days after the donation, the blood donor began feeling unwell, with dizziness, vomiting and diarrhoea. Accordingly, he went to the emergency room of a local hospital, in the evening, after work. No specific diagnosis was made when he was seen in the emergency room, but he was kept overnight for observation. The next day, he went into septic shock and the cultures of blood taken from him in the emergency room were positive for *S. aureus*. He subsequently developed disseminated intravascular coagulation and had a stormy hospital course, but survived. Soon after admission to hospital, a family member of the donor told the attending physician that he had donated bood 4 days previously. This information was transmitted to the blood manufacturer (Canadian Blood Services), who alerted the physician attending the platelet pool recipient. The *S. aureus* isolates from both the donor and the recipient were found to be identical on antibiotic sensitivity and by gene mapping, indicating that they were likely from the same source.

The important issue arising from this particular case, is the fact that had the blood donor not presented with a septic episode subsequently to his whole-blood donation, it is likely that this fatal transfusion-associated septic reaction would not have been attributed to the platelet transfusion.

Question 2

We have done three prospective studies at our Centre, evaluating the frequency of bacterial contamination of allogeneic platelet concentrates, in both random donor and apheresis platelets. In the first study, 16 of 31,610 random donor platelet concentrates were found to be contaminated with bacteria [1]. The organisms isolated were mostly skin

contaminants. Nonetheless, the true contaminant rate was estimated at 51 per 100,000 units. In this study and the next, a true positive was defined as a platelet unit of which one or more of the associated blood components again provided evidence for the presence of the same organism as that isolated from the initial sample (segment). The bacterial culturing technique involved the use of two different automated detection devices (each for a 6-month period) which tested aliquots of the platelets taken within 24 h of the time of preparation.

Because of the possibility that some organisms might not be detected on day 1, a second prospective study was done to ascertain whether day 1 and day 3 cultures were equal in sensitivity [2]. A second aspect of this latter study was to determine the number of organisms present in the contaminated platelet units evaluated. Over an 18-month period, over 16,290 units of random donor platelets were cultured on day 1. Of these, 10,065 were also available for culture on day 3. Thus, 61.8% of routinely prepared random donor platelet units were cultured on both days 1 and 3. Over the whole study period, only 11 of 26,325 units tested were found to contain true-positive contaminants. Four of the true-positive units were from day 1 cultures and 7 were from day 3 cultures. All true-positive cultures from day 1 were also positive on day 3. Thus, the day 1 true-positive prevalence was 25 per 100,000 units, whereas the day 3 true-positive prevalence was 70 per 100,000 units. This study thus indicated that the prevalence of true positives on day 3 was approximately 3-fold higher than on day 1. This implies that approximately two thirds of platelet units that contain bacteria would not have been detected by bacterial cultures done on day 1. The enumeration of the quantity of bacteria present in the positive cultures observed indicated that the number of organisms present in contaminated platelet units ranged from 10^{-3} to 10^{7} CFU/ml [2].

We also conducted a smaller prospective study in our Centre evaluating the bacterial contamination rate of apheresis platelet units. Of 6,055 units tested, 14 were found to be positive for a rate of 230 per 100,000 units [3]. The contaminated units were not evaluated further to establish whether they represented true or false positives. Based on the data from the above two studies, it is likely that at least 50% would have been false positives.

Question 3

In Canada, two decisions have been taken recently to reduce the possible risk for recipients of bacterial contamination of cellular blood products. The first measure, taken in early 1998, was to institute an improved method for the preparation of phlebotomy sites of blood donors. The method instituted was based on the studies by Goldman et al. [4] which indicated that an isopropyl alcohol scrub followed by iodine tincture was more efficacious in reducing the level of skin contaminants than the previously used povidine-iodine. The second measure, which was taken also in early 1998, was to institute universal pre-storage leucocyte reduction of all platelet units (both random donor and apheresis) distributed in Canada. The latter intervention was instituted not specifically to reduce the risk of bacterial sepsis but to improve the overall safety associated with platelet transfusions. Moreover, universal pre-storage leucocyte reduction of all red blood cell units distributed in Canada was fully implemented as of July 1999.

Acknowledgments

The author would like to thank Drs. E.C. Alport and G. Sher of Canadian Blood Services for providing the details of the case of transfusion-associated sepsis reported above and for permission to cite the incident in this International Forum.

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L. Muylle

Question 1

In Belgium, transfusion-associated reactions are reported on a voluntary basis and reporting is usually limited to serious reactions.

In 1997, 3 serious, not fatal, septic reactions due to the transfusion of bacterially contaminated blood components were noted in Flanders, the northern part of our country (6 million inhabitants).

Question 2

Since last year, microbiological cultures are systematically carried out on samples of all platelet concentrates (PLC) immediately after preparation. Over a period of 6 months, the initial culture was found positive in 63 (1.95%) of 3,297 single-donor PLC and in 148 (1.73%) of 8,537 pooled random-donor PLC. Following the finding of a positive result, 96 PLC were retested and in 3 of 35 single-donor PLC and in 29 of 61 pooled random-donor PLC, found initially positive, the first result was confirmed on a second sample.

Extrapolation of these results to the total number of prepared PLC indicates that 0.16% of single-donor PLC and 0.53% of pooled random-donor PLC are bacterially contaminated.

Question 3

For several years, special attention has been given to donor skin preparation and disinfection (two-step method).

In 1998, microbiological testing of all single-donor PLC and all pooled random donor PLC using an automated culture system (BacT/Alert 240, Organon Teknika) was started. Using a sterile technique, 20-ml samples are taken from a sampling bag immediately after preparation of the PLC; the sampling bag is an integrated part of the BC pooling and filtration system (Autostop BC, Pall Corp.) or is connected to the system using a sterile connecting device (T-SCD, Terumo). The samples are divided equally over a 40-ml anaerobic and an aerobic culture bottle for the BacT/Alert system.

The cultures are monitored continuously for 5 days. A negative microbiological culture result is required at the time of the release of a PLC. All PLC with a positive initial culture result are removed from the inventory. If the culture becomes positive after release of a PLC a call-back procedure is started. In the case that the PLC has already been transfused, the treating physician

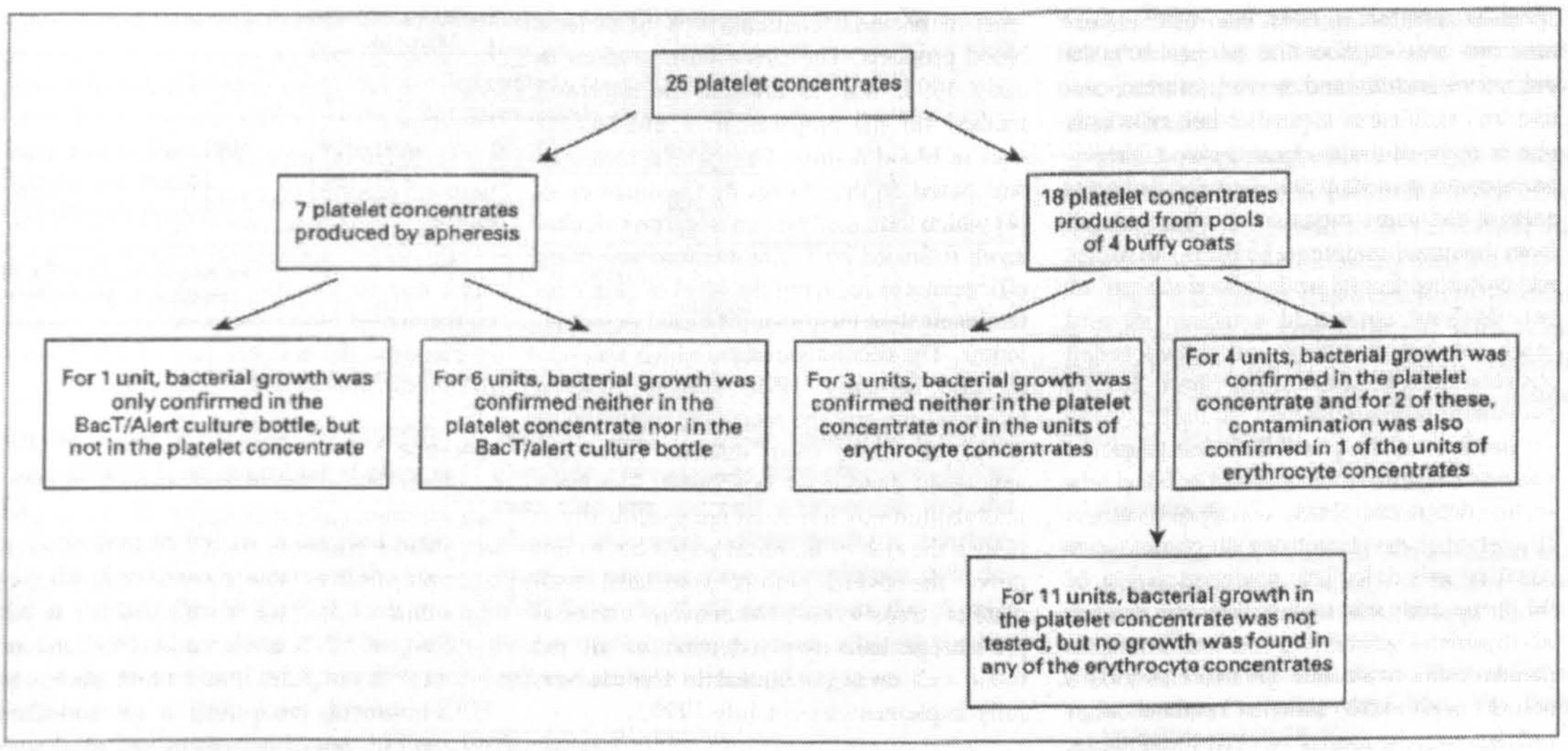

Fig. 1. Platelet concentrates giving positive results in BacT/Alert (as all samples are cultured through out the storage period of the platelet concentrates, a positive culture may appear after the unit has been transfused). Data from approximately 9,000 platelet concentrates over the period April 1, 1998 to October 1, 1999.

of the patient is informed. None of these PLC was associated with a septic transfusion reaction.

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Jens Kjeldsen-Kragh

Question 1

The frequency of transfusion-associated septic reactions is known neither in Norway nor in the clinical departments we serve.

Question 2

Since April 1, 1998 we have tested all our platelet concentrates for bacterial contamination 1 day after donation using an automated blood culture system (BacT/Alert, Organon Teknika). Over a period of $1^1/_2$ year, the percentage of contaminated concentrates ranged between 0% for apheresis units and 0.044–0.167% for BC-derived units (fig. 1). No serious adverse reactions related to bacterial contamination of platelet products were reported after we have started testing all platelet concentrates. Red cell units, however, are not tested routinely.

Question 3

Of the means listed, we used BacT/Alert (culture bottles for aerobic bacteria) to test all platelet concentrates for bacterial contamination and, in addition, we deplete all cellular blood products of leucocytes. Finally, all blood products are inspected visually.

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R. Kekomäki

The Finnish Red Cross Blood Transfusion Service collects annually approximately 350,000 units of blood from voluntary, unpaid donors, more than 40% being collected in mobile sessions countrywide, the other collections being done in fixed premises. Components are prepared in 5 centres using the same standard operational procedures and quality system. Whole blood is rapidly cooled to 20–22°C and stored at this temperature overnight (16–18 h) prior to processing. Key figures: in 1998, approximately 307,000 units of red cells (SAGM, buffy coat removed, of which 12% were leucocyte-depleted prior to further storage), approximately 122,000 units of buffy-coat-derived platelet concentrates the majority of them pools of 4 or 3; more than 80% leucocyte-depleted prior to further storage) and approximately 35,000 units of FFP were distributed to the hospitals serving a population of 5 million.

No centralised haemovigilance system is in place as yet. Our institute has, however, maintained a policy of recommending that all severe untoward effects possibly related to transfusion should be reported back to the producer of blood and its components on a voluntary basis.

Question 1

Septic reactions associated with transfusion of any blood component have been rarely reported [1]. The annual number of adverse events resembling a septic reaction reported to our centre varies from 1 to 4.

To be able to prove the association with a transfusion, a recommendation has been given to close the transfusion set immediately and disconnect it from the patient, store the

Table 1. Bacterial contamination of platelet concentrates in Finland

Platelets	Period	Positive[1] cultures, n	Units used for preparations, n	Contaminated %
Single units derived from PRP	1979–1994	50	47,085	0.11
Buffy coat-derived, pooled	1991–1996	12	9,758	0.11
Buffy coat-derived, pooled	1997–1998	39	26,464	0.14

PRP = Platelet-rich plasma.
[1] Day of testing = outdated.

bag with the closed transfusion set in refrigerator and submit it to microbial studies at the BTS.

The procedure to follow is decided upon jointly by the physicians in-charge at the hospital and at the transfusion service. Cultures of the patient's blood are done at the hospital and the results from blood component tests are confirmed by a third-party laboratory. Culturing both the suspected blood components and blood samples from the patient aims at proving or disclosing a shared origin of a bacterial contaminant. No single case has been identified during the 1990s.

Question 2

Any data on the rate of bacterial contamination of blood components are affected by the quality of the component itself (leucocyte-depleted or not), initial contamination level of the product, sample volume taken for the culture, sampling time as compared to blood donation and processing of the component, culture medium and detection system. Data on the frequency of bacterial contamination of platelet concentrates produced at our institute cover more than 20 years. The approach to use outdated components for bacterial cultures is such as to detect maximal contamination rate following an extended 'incubation' period. From 1978 to 1988 altogether 48 of 28,912 units (0.17%; whole blood, red cells and platelets) were positive. In most of them, bacteria were present in low concentration, i.e. 1–1,000/ml. One unit of red cell concentrate (n = 11,600) and 5 units of platelets were contaminated with more than 10^4/ml. 86% of bacterial strains detected were considered to be skin contaminants [G. Myllylä, unpubl. results].

The overall results of bacterial contamination of platelet concentrates between 1978 and 1998 are presented in table 1. In 1998 an inoculum of 4 ml was used in PediBact bottles and analysed in the BacT/Alert system (Organon Teknika). *Staphylococcus epidermidis* was identified in 12 of the 15 positive cultures, and 3 other coagulase-negative *Staphylococcus* strains were observed. In one case also the red cell concentrate and the plasma unit were culture-positive. Furthermore, in another case, one plasma unit derived from the same donation as the platelet product was culture-positive, whereas the red cell concentrate remained negative.

Question 3

The preventive measures taken to reduce the bacterial contamination rate of blood components have been the conventional ones: paying attention to the appearance of skin surrounding the venepuncture site: selecting only healthy skin for puncture, carefully disinfecting the puncture site, e.g., letting the disinfectant dry prior to the puncture, and emphasising an aseptic puncture technique as such. No initial blood sample has been removed to decrease the number of 'unavoidable' skin contaminants entering the blood bag. Storage time of platelet concentrates has been limited to 5 days although current platelet preparations as such may stay haemostatically active for a more extended period of time.

Red cell units and platelets are distributed only after careful visual inspection of the preparation. No endotoxin assays, microbial staining, ribosomal assays for bacteria, polymerase chain reaction or routine bacterial cultures are performed prior to distribution.

A small prospective trial was conducted in 1995 to prolong the storage time to 7 days during a holiday season. Blood samples from pooled buffy-coat-derived leucocyte-depleted platelet products were inoculated to PediBact bottles and cultured (BacT/Alert) according to manufacturer's guidelines (at least for 48 h) to screen for platelet preparations with a positive bacterial culture. Samples were drawn only from platelet concentrates with normal appearance and swirling. One of the 264 preparations, representing 1,056 units of blood, was positive. The growth *(S. epidermidis)* was evident after 11 h of culture. The product was removed from the stock. Pre-transfusion screening caused a heavy workload and complicated the logistics, including the extended quarantine period of platelets.

Blood processing after overnight storage at room temperature, as performed at our institute, has been suggested to be favourable for phagocytosis of contaminating bacteria [2].

Since it is known that a certain proportion of components is contaminated with common epidermal bacteria, improved methods to avoid contamination during venepuncture should be developed.

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Question 1

Data on the frequency of transfusion-associated septic reactions in our facility strictly relates to platelet units. We have not observed a confirmed transfusion-associated septic reaction after transfusion of other blood components. For platelets, we have had in place a prospective microbiologic surveillance program for more than 7 years which has gradually evolved over this time period (see below). During this time interval, from July 1991 to June 1998, approximately 5,600 pooled random donor units (primarily 5 units per pool) containing 1 or more 4- or 5-day-old units and 7,224 4- and 5-day-old single donor platelet units were prepared for transfusion and subsequently analyzed [1]. In the pooled random donor category, 6 pools were intercepted prior to transfusion because of pretransfusion gram stain positivity, confirmed as heavily contaminated on follow-up culture. Almost without a doubt, these instances, had they not been intercepted, would have been associated with a transfusion-asso-

ciated septic reaction. An additional 8 random donor pools and 3 apheresis units were transfused with a negative pretransfusion gram stain, but with follow-up culture exhibiting confirmed positivity. In the 3 instances with the apheresis platelets, there were no clinical signs or symptoms characteristic of transfusion-associated sepsis. However, in the 8 instances of transfused gram-stain-negative, culture-positive random donor platelet pools, 5 recipients exhibited signs and/or symptoms characteristic of transfusion-associated sepsis, including one or more of the following: fever, hypotension, positive posttransfusion blood culture. There were no deaths. Thus, for pooled random donor platelet pools undergoing surveillance, the anticipated rate of transfusion-associated septic reactions at our facility is 11 (6 + 5) transfused pools out of 5,600 or approximately one in every 500 pooled random donor platelet transfusions.

While no deaths were observed in the surveillance group described above, there have been 3 deaths since 1989 in our facility associated with platelet bacterial contamination. In 2 instances *(Enterobacter aerogenes* and *Pseudomonas aeruginosa)*, we had not yet initiated the surveillance program; in the 3rd instance *(Pseudomonas aeruginosa)*, the platelet pool was composed of platelets less than 4 days of age and thus did not qualify for the pretransfusion surveillance program. Over the 10-year period from 1989 to the present, we have transfused approximately 28,000 random donor platelet pools containing approximately 144,000 units. Hence, for all pooled random donor platelets issued at our facility over 10 years, the approximate rate of identified fatalities associated with transfusion of bacterially contaminated platelets is 1 in 9,333 platelet transfusions or 1in 48,000 random platelet units.

Question 2

Our interest in studying bacterial contamination of blood components, specifically platelets, began in 1991 when, during a 1-month period, 4 confirmed positive cases of platelet bacterial contamination were identified in our institution as follows: *Pseudomonas aeruginosa* (1), *Bacillus cereus* (2) and *Staphylococcus epidermidis* (1). A thorough investigation by the Centers for Disease Control and Food and Drug Administration revealed no inciting or predisposing factors [2, 3]. Nonetheless, because the *P. aeruginosa* platelet contamination likely contributed to the death of a patient and, 1 of the 2 *B. cereus* platelet contaminations contributed to patient morbidity in the form of lobar pneumonia requiring admission to the intensive care unit, we elected to institute, at that time, a prospective microbiologic surveillance program. The goals of this program were to:

(1) better define the actual incidence of platelet bacterial contamination, including unrecognized cases not associated with signs and symptoms of infection or transfusion reaction;

(2) assess the influence of the in vitro platelet storage interval on the frequency and magnitude of bacterial contamination, and

(3) assess the potential utility of a pretransfusion gram stain to prevent transfusion of bacterially contaminated platelets.

Initially, in the first 12 months, we performed pretransfusion gram stains and cultured all platelet pools and single donor apheresis units regardless of the storage age of the unit. In all, 3,141 consecutive random donor platelet pools (14,481 units) and 2,476 single donor apheresis units were studied. All single-donor apheresis units were sterile but 6 of the random donor pools (0.19%) were found to be bacterially contaminated, with 1 unit of 5 in the pool being the source in each case. Contaminants were *S. epidermidis* (4), *B. cereus* (1) and *S. aureus* (1) at counts of 0.5×10^2–10^{11} colony-forming units (CFU)/ml in platelet pools and 10^3–10^{13} CFU/ml in source units. The contamination rate for units transfused at ≤4 days (1.8 per 10,000) was significantly lower than at 5 days (11.9 per 10,000; $p<0.05$), as was the magnitude of contamination ($p<0.05$) [4]. Since the older platelets were shown to be at greatest risk for measurable bacterial contamination, we continued our prospective surveillance only in pools containing one or more 4- or 5-day-old units and with 4- and 5-day-old single donor apheresis units. These platelets are considered 'at risk'.

In our most recent surveillance project, noted above, a compilation of the rate of contamination in 4- to and 5-day-old random and single donor platelets over a 7-year period, July 1991 to June, 1998, a total of 28,152 random-donor units and 7,224 single-donor platelet units were studied. Fourteen random-donor units were confirmed positive for bacterial contamination (4.97/10,000) and 3 single donor units were confirmed positive for bacterial contamination (4.15/10,000). There was no statistical difference in the unit-for-unit rate of bacterial contamination between random- and single-donor units ($p = 1.0$). However, since random-donor units are pooled, the risk of contamination with random-donor platelet units increases by approximately the factor of the number of units in the pool. For example, a pool of 5 random-donor units would have 5 times the risk of bacterial contamination compared to a single-donor unit. In addition, our data demonstrate, for bacterial contamination of random-donor platelet units, statistically significant variability over time in the incidence of platelet bacterial contamination [5]. This suggests that as yet unknown inciting factor(s) may contribute to the occurrence of bacterial contamination of platelets. Finally, an additional study [6] shows no statistically significant difference in the risk of bacterial contamination in leukoreduced plateletpheresis products prepared by continuous filtration during collection compared to non-leukoreduced plateletpheresis products. This suggests that early leukocyte removal does not enhance the subsequent risk of bacterial growth in single-donor apheresis units.

Question 3

In our facility, we have utilized, as noted above, the gram stain as a measure to identify bacterial contamination of platelet units and interdict them prior to transfusion. The gram stain is limited in its utility in that it has been effective only in preventing transfusion of heavily contaminated platelet units – those units having greater than approximately 10^6 organisms/ml. The gram stain has missed many contaminated units with lower numbers of organisms. It is also more likely to miss gram-negative contamination compared with gram-positive contamination because the dark blue contrast against the light pink platelet background, present with gram-positive organisms, is lacking with gram-negative organisms. The consequence of performing a pretransfusion gram stain from an aliquot of a pool containing at least one 4- or 5-day-old platelet unit is as follows [1]:

Outcome for confirmed culture-positive platelet units		Total
RDP pools not transfused due to a positive gram stain, n		6/14
RDP pools transfused with a negative gram stain, n		8/14
No symptoms or sequelae	3/8	
No symptoms with sequelae	2/8	
Symptoms and sequelae	3/8	
SDP pools not transfused due to a positive gram stain, n		0/3
SDP pools transfused with a negative gram stain, n		3/3

RDP = Random-donor platelet unit.

Most recently, since we have not interdicted a bacterially contaminated platelet unit prior to transfusion with a gram stain in 3 years, during which time there have been 10 instances of confirmed culture positivity, we have elected to suspend the pretransfusion gram stain beginning on February 1, 1999. We will continue to gather culture surveillance on all of our transfusions containing 4- and 5-day-old units and reinstate the gram stain if quantitative culture surveillance reveals increased quantities of bacterial organisms. In the meantime, we await improved more sensitive and rapid methods for interdicting bacterially contaminated platelet units prior to transfusion.

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Question 1

No cases of transfusion-associated septic reactions in our hospital were reported in the last few years.

Question 2

According to the policy of our Institute, the storage period of apheresis platelet concentrates is limited to 72 h (3 days). Bacterial contamination was determined at the end of storage time in approximately 10% of platelet concentrates. Of 75 platelet concentrates tested 5 were contaminated.

More recently we have evaluated bacterial contamination of platelet concentrates stored for 5 days. Nineteen concentrates were tested so far and none were bacterially contaminated.

Question 3

Our Institution follows standard operating procedures for donor skin disinfection.

We remove at least 2 ml of blood when discontinuous cell separators are used.

The storage time of cell concentrates is limited to 42 days for erythrocyte concentrates, 3 days for apheresis platelet concentrates and 6 h for lymphocyte or granulocyte concentrates. For all blood cell products leaving the Institute, transfusion is recommended within 6 h.

Before delivery all blood products are visually inspected. All platelet- and red blood cell concentrates are leukocyte-depleted.

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Harvey G. Klein

We have no center-specific data for the Clinical Center regarding frequency of transfusion-associated bacterial sepsis. We rely currently on estimates supplied by the American National Red Cross (ARC) [1] concerning culture-positive units and unpublished reports from the Centers for Disease Control and Prevention (CDC). These reports estimate culture-positive red blood cells in the range of 0–0.2% and platelets between 0 and 10%. Febrile reactions associated with bacterial contamination are reported at 1/10,000 to 1/20,000 per unit transfused and fatalities at a rate of 1 death in 1 to 6 million units transfused. There has been no organized system of nationwide surveillance for bacterial contamination of blood components or for transfusion-associated bacterial sepsis. The Food and Drug Administration (FDA) requires reporting of fatalities, but most nonlethal events are likely unreported.

In December of 1997, a multicenter study for the systematic collection of data concerning bacterial contamination of blood components (BaCon Study) was initiated under the joint guidance of the American Association of Blood Banks (AABB), the ARC, the CDC, and the Department of Defense. The goals of the study include determination of the rates of bacterial contamination associated with recipient transfusion reactions, identification of the responsible microorganisms, identification of risk factors for bacterial contamination and for recipient morbidity and mortality.

To the best of my knowledge, no large coordinated intervention trial has been directed toward the problem of bacterial contamination. There are numerous small studies, however, most supported by hospital transfusion services, blood centers, and commercial enterprises. Some of these were reviewed in a conference at NIH in 1997 [2]. Current studies include investigation of ribosomal assays and nucleic acid amplification techniques. Visual inspection of blood prior to issue has long been a requirement and a standard of the AABB. Some centers use color charts to detect changes in color of red cell units that may indicate bacterial growth. Except for anecdotal reports, no data concerning the efficacy of this approach are available [3]. One center has made extensive use of gram staining of platelet concentrates and reports that this method is effective, if insensitive, practical, and inexpensive [4]. Others have not been able to implement this system as successfully, and it is not in widespread use.

Limits on duration of acceptable storage for licensed blood components are defined by the FDA and ordinarily are based on evidence of component safety and efficacy. Red cell storage, depending on the anticoagulant-preservative solution, has been limited by the bounds of red cell viability and function. Platelet storage at 22°C has been limited both by concerns for cell viability and func-

tion and for bacterial growth. I know of no collection entity that is further limiting storage time to reduce the risk of bacterial growth. Although shorter storage might indeed reduce morbidity related to bacterial sepsis, the trade-off in terms of blood availability is too great to shift the risk-benefit calculus.

About 20% of platelets and a smaller percentage of red cells are leukoreduced in the United States. Most leukoreduction is still done by filtration at the bedside. Universal leukoreduction of cellular blood components is almost certain to occur within the next several months and will most likely shift to prestorage processing by the blood collection center. While this change in processing will not be introduced to alter the frequency of bacterial contamination, it will be important to try to estimate what effect it will have on blood safety.

The issue of bacterial contamination remains one of the primary concerns of blood collectors and transfusion service scientists and clinicians. However the priority given to prior diseases, HIV, hepatitis, and emerging infections has in fact overshadowed bacterial contamination where research funding is concerned.

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Question 1

In the British Isles (excluding Scotland) surveillance of post-transfusion infections (including bacterial infections) reported to blood centres began in October 1995. Ascertainment of cases via an additional hospital reporting scheme (including Scotland) was added in October 1996. Between 1st October 1995 and 31st December 1998, 22 completed investigations into post-transfusion reactions suspected to be due to bacteria were reported to the surveillance system. Seven of these have been concluded to be due to the transfusion (table 1), including 2 (29%) where the infection was implicated in the death of the patient. For a further 15, the investigations lacked conclusive evidence of infection/contamination in the implicated unit(s) (table 2), including 1 (7%) where the infection/reaction was implicated in the death of the patient. Bacterial contamination of blood components remains suspected, although not proven (not isolated), as the cause of the reaction in some of these patients.

Table 1. Transfusion-associated septic reactions concluded (after investigation) to be due to an infected/contaminated blood transfusion (1st October 1995 to 31st December 1998)

Organism	Blood component	Symptoms	Fatal?
Bacillus cereus	platelets	transfusion reaction	no (patient died of leukaemia)
Bacillus cereus	platelets	collapsed during transfusion, recovered, unwell again later	outcome not known
Escherichia coli	platelets	bacteraemia	no
Escherichia coli	platelets	severe febrile reaction	yes
Serratia liquifaciens	red cells	endotoxin shock	no
Staphylococcus aureus	platelets	bacteraemia	yes
group B streptococcuccus	platelets	septic shock	no
Total 7			2 (29%)

Table 2. Transfusion-associated septic reactions for which investigation could not positively identify an infected/contaminated blood component[1] (1st October 1995 to 31st December 1998)

Organism	Blood component	Symptoms	Fatal?
Mixed	red cells	severe reaction	no
Clostridia sp.	red cells	febrile gangrene	no
Staphylococcus aureus	platelets	septicaemia	no
None identified	red cells	febrile, hypertension	no
None identified	red cells	pyrexia, breathlessness, hypertension	yes
None identified	red cells		no
None identified	red cells	cardiovascular collapse, respiratory arrest	no
None identified	red cells	febrile, back pain	no
None identified	red cells	severe hypertension	no
None identified	red cells	immediate febrile reaction	no
None identified	platelets	immediate reaction, hypertension, trachycardia	no
None identified	red cells	immediate breathlessness, hypertension, followed by cardiac arrest, multi-organ failure	no (patient died, but no evidence of contamination as cause of death)
None identified	platelets	transfusion reaction	no
Total 15			1 (7%)

[1] Other causes are also suspected.

Table 3. Retrospective study on monitoring time expired (TE) platelet concentrates for bacterial contamination: 1st February 1995 to 31st October 1997

Type	Total	Initially reactive	Confirmed positive
TE pooled platelets	1,547	27 (1.8%, 1 in 57)	11 (0.7%, 1 in 141)
TE single platelets	249	4 (1.6%, 1 in 62)	0
Apheresis platelets	1,005	13 (1.3%, 1 in 77)	4 (0.4%, 1 in 251)
Total	2,801	44 (1.6%, 1 in 64)	15 (0.5%, 1 in 187)

Table 4. Preventive measures adopted or under investigation in our country

Preventive measure	Practice in England	Comments
Improve donor skin preparation and/or disinfection	yes	study nearing completion national policy will follow
Removal of the first 2 ml of blood	being considered	
Limit storage time of cell concentrates	not considered	
Pre-transfusion detection of bacteria		problems with the logistics of some of these methods
Visual inspection	encouraged	
Endotoxin assays	no	
Microbiological staining	no	
Ribosomal assays for bacteria	pending	research project in progress (Bristol)
Polymerase chain reaction	no	
Culture techniques	no[1]	
Change blood processing		
– Leucocyte depletion	yes: implementation of universal leucodepletion under way	
– Disinfection of waterbath	not applicable	relevant for hospital units no waterbaths used at blood centres
– Alter period of storage prior to component preparation		some conflict with leucocyte depletion
Others		

[1] Although not formally under consideration automated culture of platelets after 1 day incubation, with 2 day extension to shelf-life of negatives (as in Sweden) is recommended by John Barbara.

Question 2

The data in table 3 have been provided by Carl McDonald from a study conducted at North London blood centre.

Question 3

See table 4.

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Halina Seyfried

Question 1

A tested of 783,954 units of blood were collected in 1998. One (0.0001%) septic fatality and 19 (0.002%) transfusion-associated septic reactions were reported to the blood transfusion service. Only red cell concentrates were involved. In 14 patients the contamination was due to bacteria often present in the skin of donors (micrococci, *Staphylococcus epidermidis*). In 18 patients the reactions were mild and severe in 1. The analysis of the fatal case revealed that it was due to a mistake of the clinician responsible for blood transfusion. Transfusion had been stopped because of the symptoms of a non-haemolytic reaction (fever up to 38.5°C, chills). The bag remained for 5 h connected with the patient and when the symptoms disappeared, the transfusion was continued and led to septic shock and death 10 h later. Blood collected 6 h after death showed *Klebsiella pneumoniae*, *Enterobacter cloacae* and *Serratia liquefaciens*. Microbiological staining and culture techniques on the fresh frozen plasma separated from the unit of whole blood did not show bacterial contamination.

Question 2

I have no data on the frequency of bacterial contamination of red cell and/or platelet concentrates as determined in vitro.

Question 3

The preventive measures adopted in our country are as follows:

- improvement of donor skin preparation and disinfection;
- limitation of storage time of red cell concentrates;
- pretransfusion detection of bacteria;
- visual inspection;
- changes in blood processing, and
- leucodepletion in about 30% of red blood cell and platelet concentrates (either buffy coat removal or filtration).

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Vox Sanguinis

State-of-the-Art Paper

Vox Sang 2000; 78 (suppl 2): 291–295

The Serious Hazards of Transfusion (SHOT) Initiative: The UK Approach to Haemovigilance

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Introduction

Blood transfusion is a widely used therapy in hospital practice, with over 3 million components issued annually in the United Kingdom (UK) and Ireland. In the early 1990's, there was a growing awareness among UK transfusion specialists, haematologists and other clinicians that there was little information on the safety of the whole transfusion process from blood component production in a Transfusion Centre to administration at the bedside. Major policy decisions had to be reached, and clinical guidelines produced, without a sound basis of epidemiological and statistical information. As suppliers of therapeutic products, UK Transfusion Services recognised their obligation to understand the magnitude of patient risk caused by their products. At the same time, reports from the UK and elsewhere [1,2] suggested that hospital errors in patient identification were a major source of transfusion-related morbidity and mortality. To analyse residual risks of transfusion, a voluntary reporting system for major transfusion complications – the Serious Hazards of Transfusion (SHOT) scheme – was launched in November 1996 [3].

SHOT: Aims, organization and reporting system

Aims

SHOT works as a confidential reporting system which aims to collect data on serious adverse events of transfusion of blood components, and to make recommendations to improve transfusion safety. Through the participating Royal Colleges and professional bodies, SHOT findings can be used to (1) inform policy within transfusion services and at Department of Health level, (2) improve standards of hospital transfusion practice, (3) aid production of clinical guidelines for the use of blood components, (4) educate users on transfusion hazards and their prevention, and (5) provide a 'rapid alert' of clusters of existing or new hazards which may emerge. This year, SHOT has joined the Internet, and you can find us at http//www.shot.demon.co.uk.

Organisation

The strategic direction of SHOT comes from a Steering Group with wide representation from Royal Colleges and professional bodies representing medical, nursing and laboratory staff. SHOT was affiliated to the Royal College of Pathologists in November 1997. The operational aspects of the scheme are the responsibility of a Standing Working Group, which is accountable to the Steering Group. SHOT is therefore entirely professionally driven and organised, with no direct formal links either to government or regulatory agencies. However, the Health Service Circular 1998/224

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'Better Blood Transfusion' sent from the National Health Service Executive to all hospitals, requires a clear commitment to SHOT reporting and to changes in practice resulting from SHOT observations and recommendations.

Reporting System

SHOT invites reports of major adverse events surrounding the transfusion of single or small pool blood components (red cells, fresh frozen plasma (FFP), methylene blue FFP and cryoprecipitate). It does not cover complications of fractionated plasma products; as licensed medicinal products, these are already covered by the 'Yellow Card' system of the Medicines Control Agency. However, for purposes of comparison SHOT also invites reports on complications of solvent-detergent FFP, a pooled licensed product. Hospitals report events under the following categories:

(1) incorrect blood component transfused, whether or not any harm results. This includes blood intended for another patient, or a component which does not meet the requirements of the patient
(2) acute transfusion reaction (up to 24 hours)
(3) delayed transfusion reaction (beyond 24 hours)
(4) transfusion-related acute lung injury (TRALI)
(5) post-transfusion purpura (PTP)
(6) transfusion-associated graft-versus-host-disease (TA-GVHD)
(7) bacterial contamination
(8) post transfusion viral infection
(9) other post-transfusion infection e.g. malaria
(10) incidents associated with either autologous pre-donation or return of any type of autologous blood.

At hospital level, hazards are reported to the local haematologist responsible for transfusion. Suspected cases of transfusion transmitted infection are then reported to the supplying blood centre; this is essential to ensure rapid withdrawal of other implicated components and appropriate donor follow-up. These cases are then reported by blood centres to the Public Health Laboratory Service Communicable Disease Surveillance Centre (PHLS CDSC) post-transfusion infection surveillance system. Non-infectious hazards are notified directly from hospitals to the SHOT office on an 'initial report' form. On receipt of a report, the assistant national co-ordinator allocates a number to the case, then issues a detailed follow-up questionnaire specifically designed for each hazard. Once complete, the information in the questionnaire is entered in an anonymised way on to the SHOT database, and the paper record shredded. Thus there can be no trace back to individual cases.

An Annual Report and separate Summary of Findings and Recommendations combine the data from the infectious and non-infectious arms of the reporting system. Both are sent to all hospitals, the aim being for the Summary to be widely distributed to all types of hospital staff involved in handling blood. Most hospitals in the UK now have a Transfusion Committee, which has a useful co-ordinating role in implementing SHOT findings.

Key findings 1996-1999

The third Annual SHOT Report[5] was launched on 7 April 2000 to coincide with the World Health Organisation's World Health Day, which had as its theme 'Blood Safety'. Results from the first three annual reports [5-8] are summarised below.

Overview

Of 424 eligible hospitals, 94 submitted 169 reports during the first year, and 112 submitted 197 reports during the second year, an increase of 16.5%. "Nil to report" cards, introduced in the second year, were submitted by 164 hospitals, bringing overall participation to 65%. In the third year, of 432 eligible hospitals, 132 submitted 252 reports, an increase in reports of 27.9% compared with the previous year. Including 204 hospitals which sent "nil to report" returns, overall participation in the third year was 77.8%. SHOT reporting now covers >90% of all red cell usage in the UK.

The breakdown of reports by type is shown in the Figure. In particular, we have drawn attention to the problem of 'wrong blood transfused' incidents which in each of the 3 years have comprised over half the cases reported: 335/618 (54.2%) in total. Transfusion transmitted infections account for a very small proportion of reported post-transfusion complications - 3% - (n=19). Of 584 cases analysed over 3 years, there were 28 deaths and 114 cases of major morbidity, defined as intensive care admission or possible long term sequelae (Table 1).

Incorrect blood or component transfused

Of the 335 reported episodes in which a patient was transfused with the wrong blood component, 97 were ABO incompatible, leading to 4 deaths and 29 cases of immediate major morbidity. There were 13 cases of potential RhD sensitisation in young female patients. Notably, the errors in each of 313 analysed cases of incorrect transfusion consisted of a sequence of one to 7 procedural failures to detect incorrect identity of blood or patient, leading to transfusion to the wrong patient. Errors occurred at all stages of the transfusion process but a key source of error was collection of the wrong blood from the blood bank refrigerator. Blood was frequently taken without a formal identity check against the patient's case record. In addition, administration of a blood component to the wrong patient usually involved failure of the bedside checking process to detect discrepancy in blood and patient identity (n=140). In 35 cases, the patient had no identity wristband. Prescription, request or blood sampling errors (n=61) included four incidents of transposition of blood grouping samples at the patient's bedside. Two of these, one fatal, involved the use of pre-labelled sample tubes, contrary to existing British Committee for Standards in Haematology (BCSH) guidelines [9]. Laboratory errors (n=95) included failure to consult/heed historical records, as well as incorrect grouping, cross matching and labelling.

Immune complications of transfusion

These were reported in five categories (acute and delayed reactions, TRALI, PTP and TA-GVHD). These cases were unpredictable and generally did not reflect poor practice. However, with the exception of haemolytic events, reactions were investigated inconsistently, and it was not always possible to determine the cause of the reaction. Seven reports were received of a hypotensive reaction to components passed through a bedside leucocyte filter [10]. Over 3 years, there have been 39 cases of TRALI following transfusion of red cells and platelets, as well as FFP. PTP is almost certainly underreported, but cases were investigated and managed appropriately. Of 10 cases of TA-GVHD, all fatal, 4 had B cell lymphoproliferative disorders not covered by current UK guidelines for irradiated components.

Transfusion transmitted infection

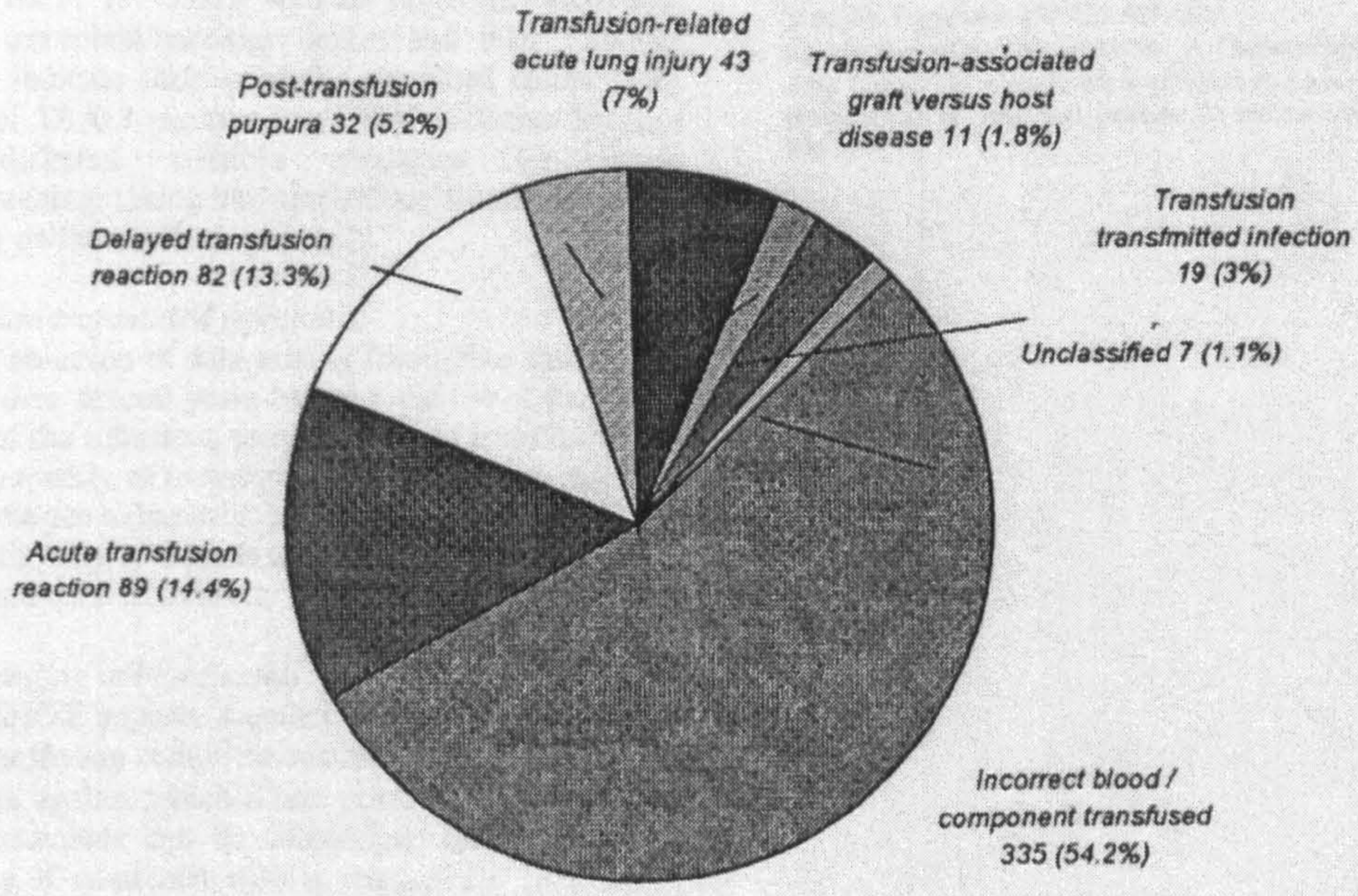
Of 94 suspected cases, only 19 (20%) were confirmed to be related to the transfusion. Eleven cases (one hepatitis A infection, one malaria, nine bacteraemias) were due to infections for which no testing of donations is performed, while six cases (four hepatitis B, one hepatitis C, one HIV) were due to donations taken during the marker negative "window period" after recent infection. There were 2 further cases of hepatitis C infection; one a newly reported case of hepatitis C was in a patient who received a blood transfusion before the introduction of donor screening in 1991, and another due to laboratory error in hepatitis C testing – corrective and preventative action was subsequently put in place. Of the nine bacterial cases, two involved red cells, contaminated with *Serratia liquefaciens* and a fatal *Yersinia enterocolitica* transmission. The remaining six involved platelet transfusions, comprising a fatal case of Staphylococcus aureus, isolated from the donor's skin and nose, two cases of *Escherichia coli* (one fatal), two cases of *Staphylococcus epidermidis* and one of *Bacillus cereus*. The other fatality caused by infection was due to cerebral malaria after transmission of *Plasmodium falciparum* from a donor who lived in a malarious area as a child and who had visited (a different) malarious area within the previous four years. This rapidly led to amendments to selection criteria for donors.

Table 1. Morbidity and mortality related to transfusions in fully analysed cases 1996 – 1999 (n=584)

Detail	Total	Incorrect component transfused	Major acute transfusion reaction	Major delayed transfusion reaction	Post-transfusion purpura	TA-Graft versus host disease	Transfusion related acute lung injury	Transfusion transmitted infection	Un-classified
Death attributed to transfusion	28	4	1	4	1	10	4	4	0
*Death possibly due to transfusion	9	2	2	0	1	0	4	0	0
Major morbidity	114	44	3	17	5	0	31	14	0
Minor / no morbidity	425	259	75	59	26	0	0	1	5
Outcome unstated	8	3	3	0	0	0	0	0	2
Total	584	312	84	80	33	10	39	19	7

* The category "Death possibly due to transfusion" was introduced for the 1998 / 99 reporting year.

Figure 1. Overview of 618 cases for which initial reports forms were received 1996 - 1999



Key recommendations and associated new initiatives in blood safety

Incorrect blood or component transfused

Getting "the right blood to the right patient in the right place at the right time" is a complex chain from patient blood sampling through laboratory testing to bedside administration. The three SHOT reports have emphasised that multiple errors may occur at all stages of the process. Following the first SHOT report, the BCSH developed a very useful guideline on blood administration [1]. A number of recommendations in this guideline are in line with those in the SHOT reports, including the need for strict procedures to avoid confusion between patients at the time of sampling, minimum formal identification requirements when blood is collected from the hospital blood bank, the importance of bedside checking procedures, the provision of identity wristbands, ensuring that special requirements of patients are met (e.g. for irradiated or CMV negative blood), consultation of the historical record in the hospital blood bank and formal recording of telephone requests. It is essential that this guideline is disseminated widely within hospitals. If used as the basis for a comprehensive staff training (and retraining) programme, this guideline offers sound practical advice on how transfusion errors can be reduced. However, to reduce 'wrong blood' episodes to the vanishingly low level of viral transmission now seen, innovative computing developments to ensure correct blood/patient identity would be required. These systems would have other major advantages, e.g. in reducing errors in drug administration. The NHS IT strategy should take a lead in assessing this area of new technology.

Immune complications of transfusion:

Clinicians should continue to report all types of serious adverse event following transfusion, as this may act as an early warning of adverse effects of novel techniques and processes (e.g. leucocyte depletion, virus inactivation, drug/product interactions). Any possible impact of universal leucocyte depletion of the blood supply (achieved in November 1999) on TA-GVHD incidence will take several years of further monitoring to emerge, so it is critical that full

details of all cases are returned to SHOT. A standard protocol for the investigation of suspected TA-GVHD cases should be developed, and extension of the indications for irradiated components to eliminate TA-GVHD considered. A national card, designed by the BCSH, is available to be issued to patients at risk of TA-GVHD who are receiving shared care between a transplant/oncology centre and their referring hospital, to indicate their need for irradiated components. Prevention of TRALI requires that UK Transfusion Services consider different possible strategies for donor selection/screening, taking into account logistics, effect on the blood supply and cost-effectiveness.

Transfusion transmitted infections:

National collation of data arising from these cases needs to continue over several years before a picture of the extent and nature of the infectious complications of transfusion can emerge. The quality of investigation of transfusion reactions suspected to be due to bacteria is variable. National guidelines on the investigation of these cases are currently being revised following comments from users.

Priority setting in blood safety:

The 3 SHOT reports together offer a comprehensive picture of transfusion complications in the UK. This provides powerful data against which future priorities for transfusion safety enhancements can be considered. However, this is possible only if combined with a strategy for considering transfusion risks together, and setting priorities for allocation of resources. There remains a need for an overarching approach to decision making in relation to blood safety. A national unified body is needed, with appropriate relevant expertise and representation from professional bodies which can prioritise new initiatives in blood safety. This should be complemented by a parallel initiative on appropriate prescription of blood.

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Accepted for publication 22 June 2000

doi:10.1053/jinf.2000.0722,
available online at http://www.idealibrary.com on IDEAL®

The Prevalence of Hepatitis B Infection in Adults with no Recognized Increased Risk of Infection

Sir,

In the U.K., it is under debate whether immunization for hepatitis B (HBV) infection should be targeted at individuals with a recognized increased risk of infection (as currently recommended[1]) or given universally (as recommended by the WHO).[2,3] The additional benefit of universal immunization above a well implemented selective programme is that it provides direct protection to individuals with no recognized increased risk of infection. Estimates of the prevalence of infection in these individuals are therefore helpful when considering universal immunization, as they provide a measure of the maximum benefit of extending immunization to these groups. HBV testing of large numbers of low risk individuals is, however, rarely performed.

Blood donations are collected from individuals with no recognized lifestyle risk for blood-borne infections and are tested for hepatitis B surface antigen (HBsAg) in order to exclude infectious donations from the blood supply. The prevalence of HBsAg is low: 0.03% of new donors were found to be HBsAg positive in England and Wales during 1998.[4] Testing for hepatitis B core antibody (anti-HBc) additionally identifies individuals who have had HBV infection and are now HBsAg-negative. During 1995, the National Blood Service in the London and South-east region of England conducted a project that involved testing more than 100 000 blood donors for anti-HBc.[5] Information about the donors tested during this project has been collated and used to estimate the prevalence of HBV infection in adults with no recognized increased risk of infection who are therefore unlikely to receive selectively offered HBV immunization in the U.K.

Data were collected from two blood centres (A: East Anglia, B: South Thames) about the age, sex and country of birth (centre B only) of each donor tested during the period of the anti-HBc project, and about anti-HBc test results from the project's records. Samples reactive to initial testing by Abbott Corzyme (Abbott Laboratories, North Chicago, U.S.A.) were further tested by Abbott IMXcore and Abbott IMX hepatitis B surface antibody (anti-HBs) test, and, if anti-HBs negative (or below 0.1 IU/ml), by Ortho anti-HBc ELISA (Ortho Diagnostics, Raritan NJ, U.S.A.) to exclude false positives.[5] Anti-HBc positive results were linked to the appropriate donor data by matching of unique record numbers. As not all (90%) donations collected during the period of the project were tested for anti-HBc, the donor dataset was scaled, maintaining the age and sex distribution, to the number of anti-HBc tests performed for the calculation of prevalence estimates as appropriate.

The overall prevalence of anti-HBc was 0.57%. Adjustment for the depletion of infected individuals from our anti-HBc tested cohort due to previous HBsAg testing (89% of donations are collected from individuals who have donated blood previously) slightly increased the overall prevalence estimate to 0.59% (by addition of $0.03\%^4 \times 89\% \times 104\,287 = 28$ infections). The prevalence increased with age ($P < 0.00001$) and was higher in donors to centre B ($P < 0.005$). Males had a higher prevalence (0.66%) than females (0.46%) ($P < 0.0001$) (Fig. 1). The prevalence amongst centre B donors born in the U.K. (343/70,203, 0.49%) was lower than that in donors born outside the U.K. (97/3197, 3.03%) ($P < 0.00001$) and increased with age

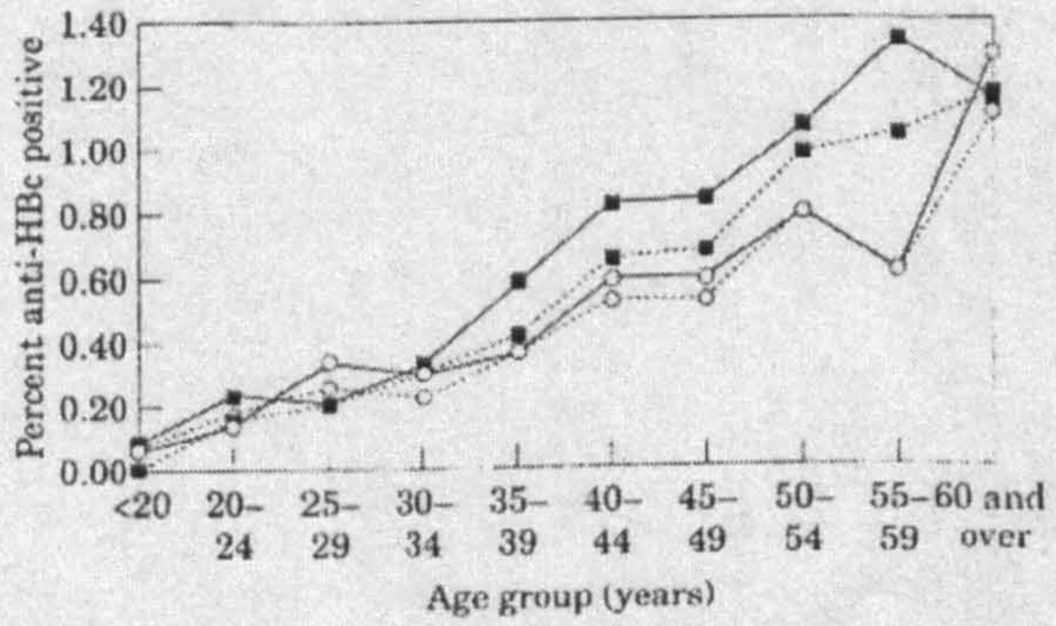

Figure 1. Anti-HBc prevalence in blood donors. (-○-) Females: UK-born donors (centre B only) 139/32 889, 0.42%. (-●-) Males: UK-born donors (centre B only) 204/37 314, 0.55%. (-▽-) Females: all donors (centres A and B) 234/50 372, 0.47%. (-■-) Males: all donors (centres A and B) 358/53 915, 0.66%.

($P<0.00001$) (Fig. 1). The prevalences observed amongst donors born in regions with more than 200 donors tested were: Western Europe 2.59% (41/1581), Australasia 2.14% (5/234), India/Pakistan/Bangladesh and other Asian 3.71% (17/458), sub-Saharan Africa 4.91% (20/407).

The prevalence of hepatitis B infection in this population was low and the number of infections that could be prevented only by universal vaccination of UK-born individuals appears to be extremely small. Some of these infections might be prevented by selective immunization of occupational groups who are not excluded from donating, and some through reduction in secondary transmission from other selectively immunized groups.

Infections in non-UK-born individuals may have been acquired prior to arrival in the U.K., or reflect higher risk of infection amongst sub-groups of the U.K. population with a higher prevalence of carriage.

HBV infection was more frequent in donors to the London-based centre – even after excluding those donors born outside the U.K. Increasing prevalence with age may be due partly to accumulating exposures to infection and partly to HBV infection having been more common in the past. The prevalence in younger adults is more likely to reflect recent exposure levels (over 80% of reported acute infections, 1991–1997, were aged under 45 years).

Acknowledgements

We thank all the staff in the NBS-L&SE involved with the anti-HBc project on which this study was based and Robin Lambert for providing data.

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Accepted for publication 17 July 2000

CDR WEEKLY

Communicable Disease Report

Volume 7
Number 29
18 July 1997
ISSN 1350-9357

Surveillance of viral infections in donated blood

Testing donated blood for markers of infections that can be transmitted to recipients is important in maintaining the safety of transfused blood. The National Blood Authority (NBA), the Welsh Blood Service, and the PHLS Communicable Disease Surveillance Centre (CDSC), began collaborating to provide national surveillance of infections detected in donated blood in October 1995. They also collaborate in the voluntary confidential system known as 'Serious Hazards of Transfusion' for reporting all major complications of blood transfusions in the United Kingdom and the Republic of Ireland, which was launched in November 1996[1]. Data on markers of hepatitis B virus, hepatitis C virus (HCV), and HIV infections in donated blood collected in England and Wales during 1996 are published in this issue (see page 258).

The overall rates of infected donations in England and Wales in 1996 were low and rates were much lower in donations from repeat donors than in new donors. Most donations of blood (88%) came from repeat donors. Rates were similar to those in other countries in western Europe. HIV antibodies were detected in 0.79 per 100 000 donations tested in England and Wales in 1996, compared with 2.41 in France (1995), 1.49 in Germany (1993), 1.03 in Denmark (1995), and 0.28 in Finland (1995)[2]. HCV antibodies were detected in 0.06% of donations from new donors in England and Wales in 1996, compared with 0.28% in France (1994), 0.16% in Germany (1995), 0.05% in Finland (1995), and 0.04% in Denmark (1995)[3]. Differences in the prevalence and incidence of infections in the general population and differences in the recruitment and selection of donors affect the rates of infection in donations of blood. The tests that are used also affect rates: in the United Kingdom, blood donations are tested for hepatitis B virus surface antigen (HBsAg) whereas in Denmark and France, blood donations are tested for HBsAg and antibody to hepatitis B core antigen.

On rare occasions infected donations may enter the blood supply because the infected donations do not have the serological marker used to test for infection[4] or the test fails to detect the marker. The appropriate blood centre should be informed immediately if such an event is suspected. Components can then be withdrawn and investigation of the source of infection can prevent further transmission of infection.

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Public Health Laboratory Service

18 July 1997 Communicable Disease Report Vol 7 No 29

Surveillance of viral infections in donated blood: England and Wales, 1996

Donated blood is collected from volunteer adult donors who do not acknowledge any medical conditions, travel history, or behaviours, that are known to be associated with an increased risk of bloodborne infections. Donated blood is tested currently for hepatitis B virus surface antigen (HBsAg), hepatitis C virus antibodies (anti-HCV), HIV antibodies (anti-HIV), and treponemal antibodies. Donations are released to the blood supply only if none of these markers of infection are detected. Donors who have any of these markers are informed of their infection, are told to stop donating blood, and are referred to appropriate services for further care. Repeat blood donors have attended to donate blood previously but their previous donations may not have been tested for some of these markers.

A total of 406 donations (15.99 per 100 000 donations) collected by the English and Welsh Blood services during 1996 had markers of viral infections (table). Of these 406 infected donations, 262 (65%) had anti-HCV, 124 (31%) had HBsAg, and 20 (5%) had anti-HIV. New donors contributed 12% of all blood donations, but 76% of infected donations.

Blood donations have been tested for anti-HIV since 1985 and for anti-HCV since 1991. The annual rates of these two markers in donations of blood from new and repeat blood donors are shown in figures 1 and 2. The rate of infected donations from repeat donors falls after new or improved tests are introduced, because repeat donors with the marker are detected and stop donating blood. HBsAg and anti-HCV were 2.8 and 1.9 times respectively more common in newly tested male donors than newly tested female donors in 1996 (chi squared test $p<0.001$ for both markers). The mean age of newly tested donors who had HBsAg was 36.7 years (95% confidence interval (CI) 35.6 to 37.8), for anti-HCV it was 33.2 years (95% CI 30.9 to 35.5), and for anti-HIV it was 28.3 years (95% CI 22.8 to 33.7).

Table Markers of infection detected in blood donations: England and Wales, 1996

	HBsAg	anti-HCV	anti-HIV	All three markers
All donations	124	262	20	406
per 100000 donations tested	4.88	10.32	0.79	15.99
1 in x donations	20 479	9692	126969	6 255
Donations from new donors	109	190	9	308
per 100000 donations tested	36.80	64.16	3.04	104.00
1 in x donations	2717	1559	32906	962
Donations from repeat donors[1]	15	72	11	98
per 100000 donations tested	0.67	3.21	0.49	4.37
1 in x donations	149 549	31 156	203930	22890

[1] May include donations from repeat donors newly tested for markers of infection

Figure 1 Blood donations with anti-HIV: England and Wales, 1 January 1986 to 31 December 1996

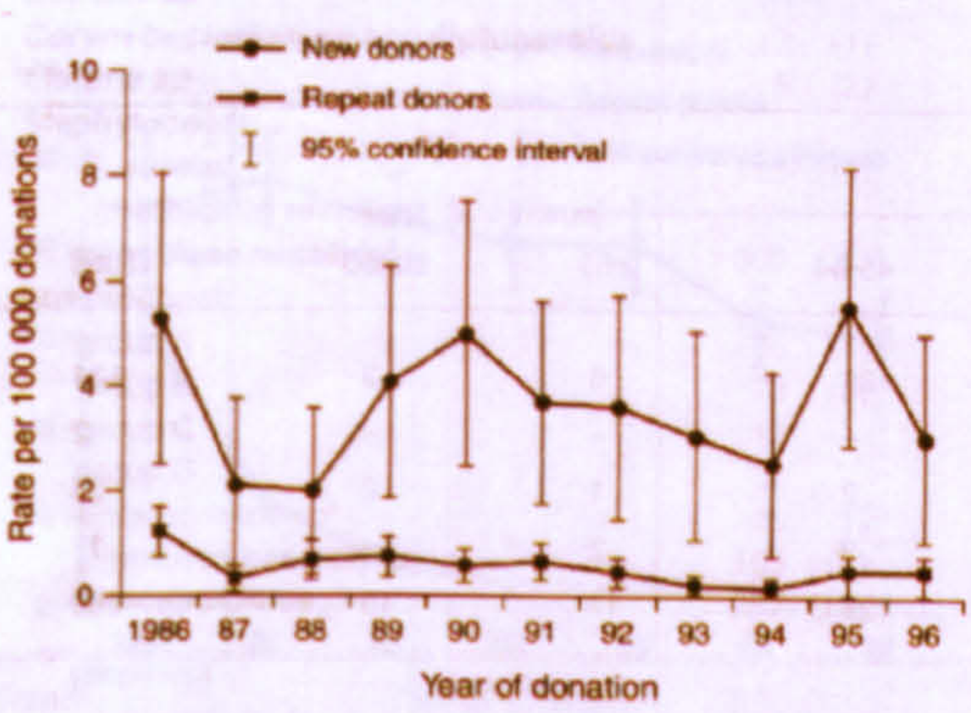


Figure 2 Blood donations with anti-HCV: England and Wales, 1 September 1991 to 31 December 1996

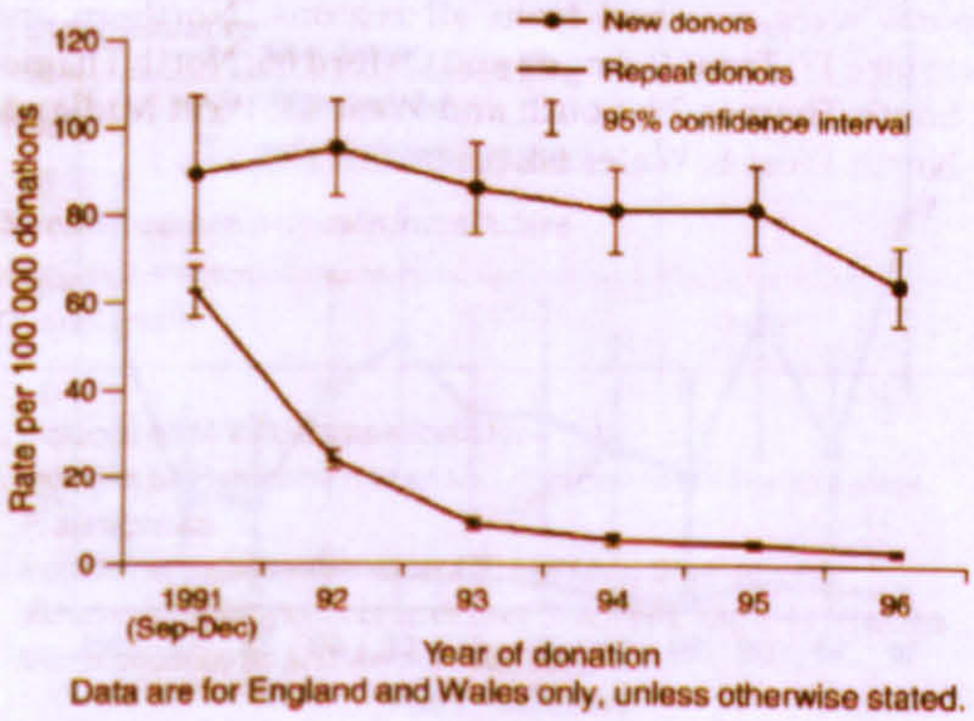
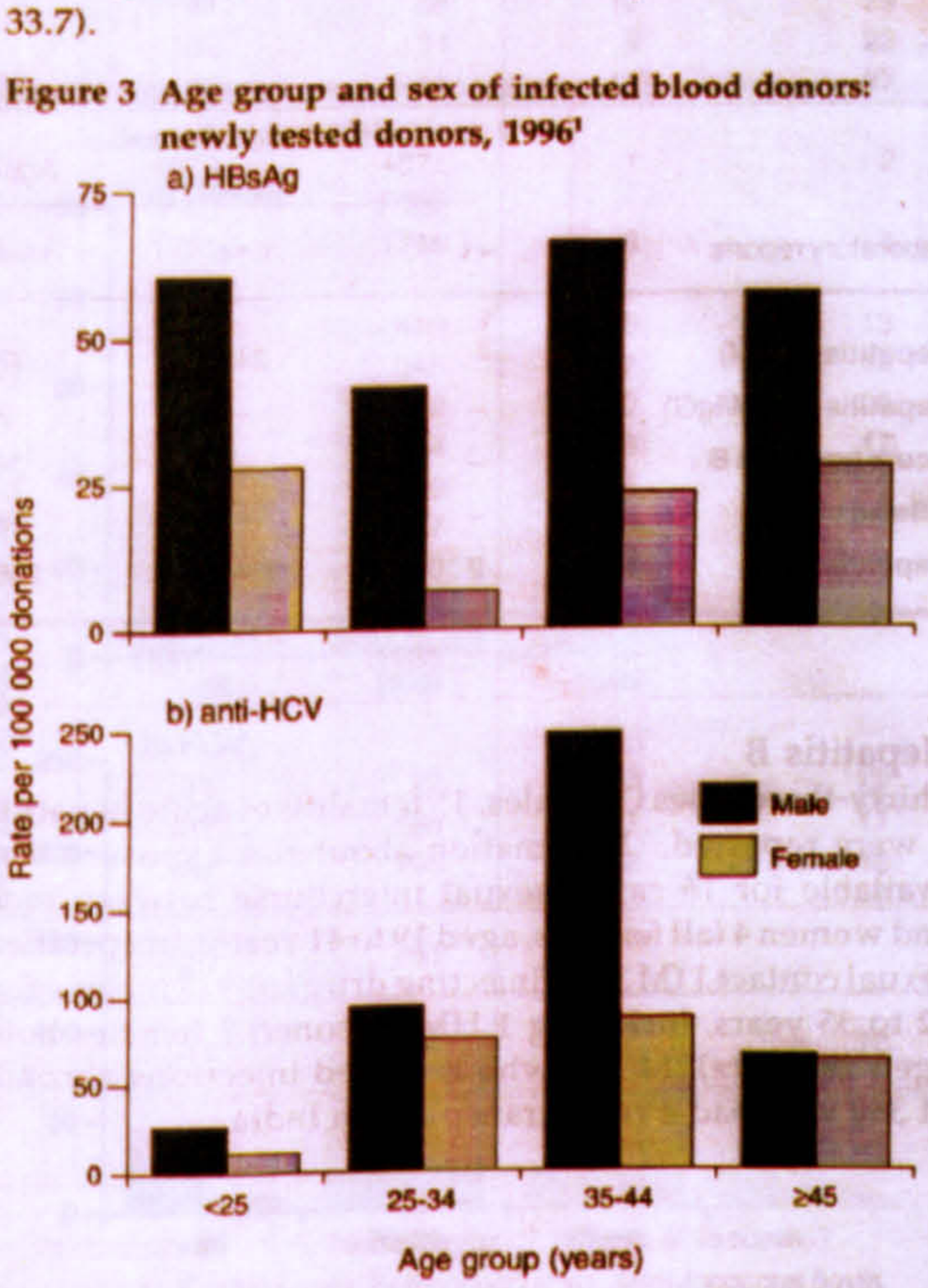


Figure 3 Age group and sex of infected blood donors: newly tested donors, 1996[1]



[1] Rates adjusted for underreporting by multiplying the denominator estimate for each age and sex group by the proportion of all detected infections for which information on age and sex has been reported

Data are for England and Wales only, unless otherwise stated. Weekly numbers are provisional and should not be used to indicate trends.

Registered as a newspaper.

9 Oct 1998 Communicable Disease Report Vol 8 No 41

Surveillance of viral infections in donated blood: England and Wales, 1997

Blood for transfusion in England and Wales is collected from adult volunteer donors who do not acknowledge any medical conditions, travel history, or behaviours known to be linked to an increased risk of bloodborne infections. Donated blood is tested currently for hepatitis B virus surface antigen (HBsAg), hepatitis C virus antibodies (anti-HCV), HIV antibodies (anti-HIV), and treponemal antibodies. Donations are released to the blood supply only if none of the markers is detected. Donors who have any of these markers are informed of their infection, told to stop donating blood, and referred to appropriate services for further care. Earlier donations from repeat blood may not have been tested for some of the markers listed: testing for anti-HIV began in 1985 and for anti-HCV in 1991.

A total of 389 donations (14.57 per 100 000 donations) collected by the English and Welsh blood services in 1997 had markers of viral infections (table). Sixty-one per cent (236/389) of the infected donations had anti-HCV (figure 1), 31% (124) HBsAg, and 7% (29) anti-HIV (figure 2). New donors contributed 11% of all blood donations, but 74% of infected donations. The rate of anti-HIV prevalence in donors in 1997 was higher than in with previous years.

Table Markers of infection detected in blood donations: England and Wales, 1997

	HBsAg	anti-HCV	anti-HIV	Any of these three markers
All donations	124	236	29	389
per 100 000 donations tested	4.64	8.84	1.09	14.57
1 in x donations	21 535	11 315	92 079	6864
Donations from new donors	93	172	21	286
per 100 000 donations tested	33.08	61.19	7.47	101.74
1 in x donations	3023	1 634	13 386	983
Donations from repeat donors*	31	64	8	103
per 100 000 donations tested	1.30	2.68	0.33	4.31
1 in x donations	77 071	37 331	298 649	23 196

* May include donations from repeat donors newly tested for markers of infection

This is being investigated, although the rate is based on a small number of anti-HIV positive donations.

HBsAg and anti-HCV were detected more often in newly tested male donors than in newly tested female donors in 1997 (2.5 and 2.3 times respectively, chi squared test $p<0.001$ for both markers) (figure 3). Newly tested donors with anti-HCV had a mean age of 38.4 years (95% confidence interval (CI) 37.1 to 39.7), which was older than newly tested donors with HBsAg (34.6 years; 95% CI 32.3 to 36.9) and newly tested donors with anti-HIV (29.6 years; 95% CI 25.9 to 33.4).

Figure 1 Blood donations with anti-HCV: England and Wales, 1 September 1991 to 31 December 1997

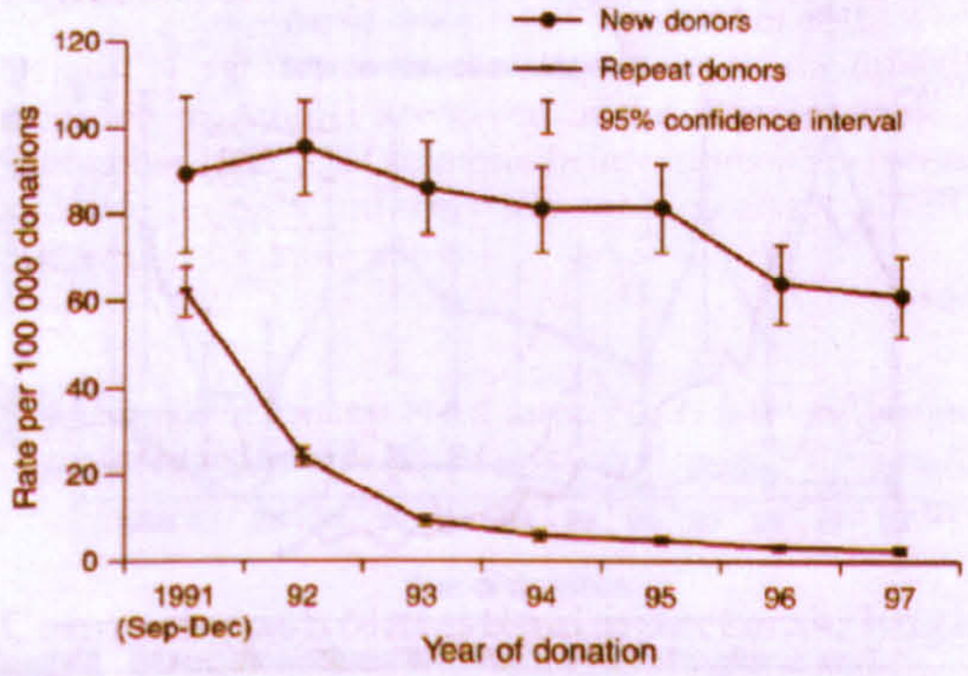


Figure 2 Blood donations with anti-HIV: England and Wales, 1 January 1986 to 31 December 1997

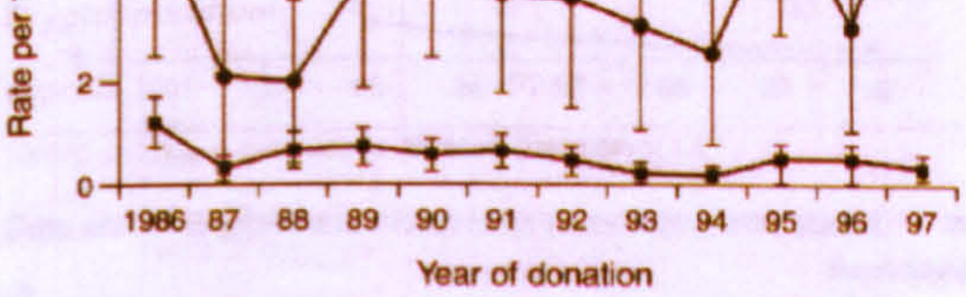
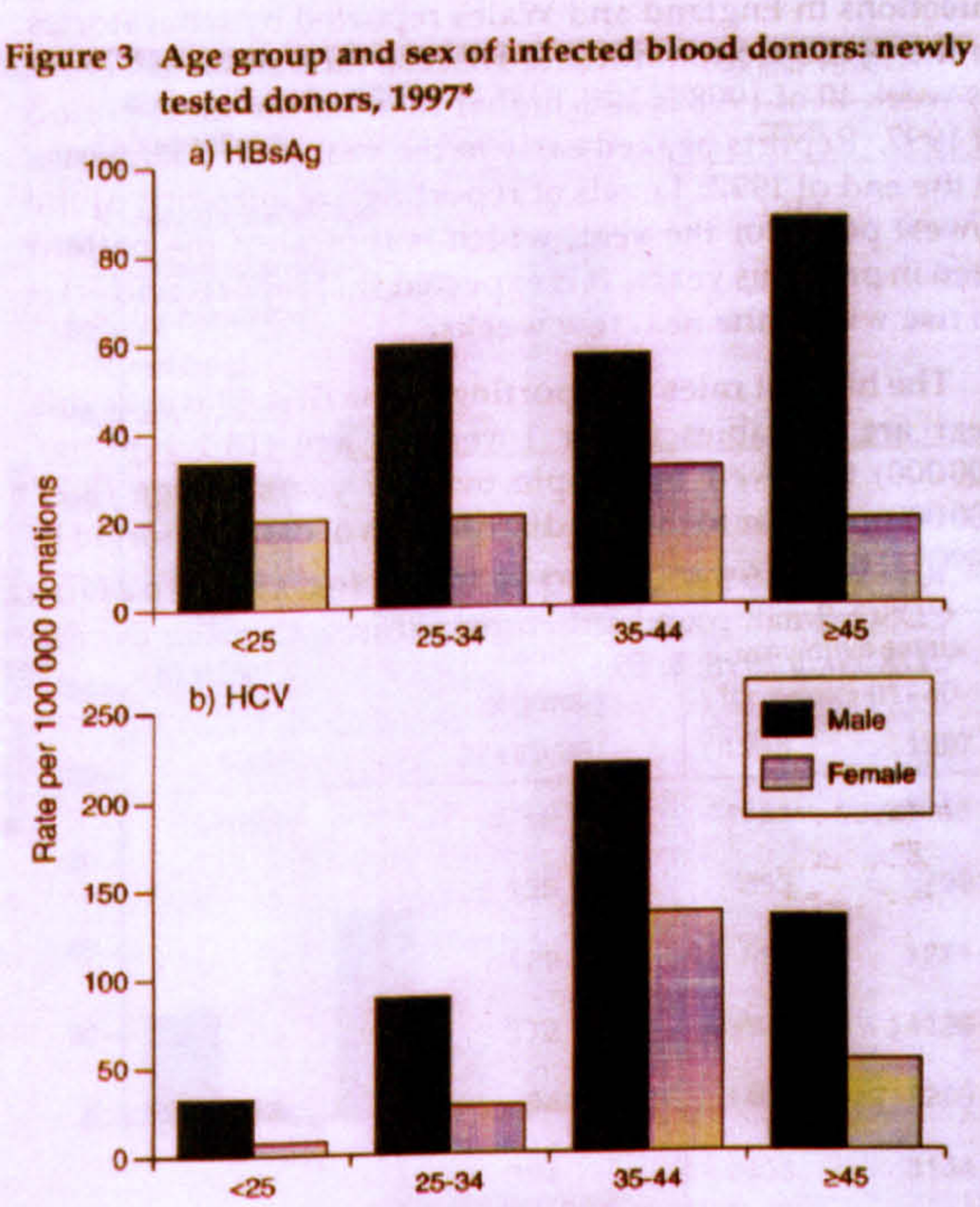


Figure 3 Age group and sex of infected blood donors: newly tested donors, 1997*



* Rates adjusted for underreporting by multiplying the denominator estimate for each age and sex group by the proportion of all detected infections for which information on age and sex has been reported

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Registered as a newspaper.

17 Sep 1999 Communicable Disease Report Vol 9 No 38

Surveillance of viral infections in donated blood: England and Wales, 1998

Donated blood is collected from volunteer adult donors who do not acknowledge any medical conditions, travel history, or behaviours that are known to be associated with an increased risk of bloodborne infections. During 1998 all donated blood was tested for hepatitis B virus surface antigen (HBsAg), hepatitis C virus antibodies (anti-HCV), HIV antibodies (anti-HIV), and treponemal antibodies. Donations are released to the blood supply only if no markers of infection are detected. Donors in whose blood any detected markers of infection are found are informed of their infection, told to stop donating blood, and referred to appropriate services for further care. Repeat blood donors have attended to donate blood previously but their previous donations may not have been tested for some of these markers.

A total of 313 donations (12.51 per 100000 donations) collected by the English and Welsh blood services during 1998 had markers of viral infections (table). Fifty-nine per cent of these infected donations (184/313) had anti-HCV, 35% (109) had HBsAg, and 6% (20) had anti-HIV. New donors contributed 11% of all blood donations, but 71% of infected donations. Blood donations have been tested for anti-HIV since 1985 and for anti-HCV since 1991. The annual rates of these two markers in donations of blood from new and repeat blood donors are shown in figures 1 and 2. The higher rate of anti-HIV prevalence observed in new donors in 1997 relative to previous years was not repeated in 1998. HBsAg and anti-HCV were 1.9 and 2.2 times commoner, respectively, in newly tested male donors than newly tested female donors in 1998 (chi squared test $p<0.01$ for both markers). Newly tested donors with anti-HCV (mean age 37.9 years; 95% confidence interval (CI) 36.7 to 39.2) were slightly older than newly tested donors with HBsAg (mean age 36.5 years; 95% CI 34.3 to 38.7) and newly tested donors with anti-HIV (mean age 31.5 years; 95% CI 27.3 to 35.7).

Table Markers of infection detected in blood donations: England and Wales, 1998

	HBsAg	anti-HCV	anti-HIV	Any of these three markers
All donations	109	184	20	313
per 100000 donations tested	4.36	7.35	0.80	12.51
1 in x donations	22954	13598	125099	7994
Donations from new donors	93	117	11	221
per 100000 donations tested	34.89	43.90	4.13	82.91
1 in x donations	2866	2278	24231	1206
Donations from repeat donors*	16	67	9	92
per 100000 donations tested	0.72	3.00	0.40	4.12
1 in x donations	139715	33365	248383	24298

* May include donations from repeat donors newly tested for markers of infection

Figure 1 Blood donations with anti-HIV: England and Wales, 1 January 1986 to 31 December 1998

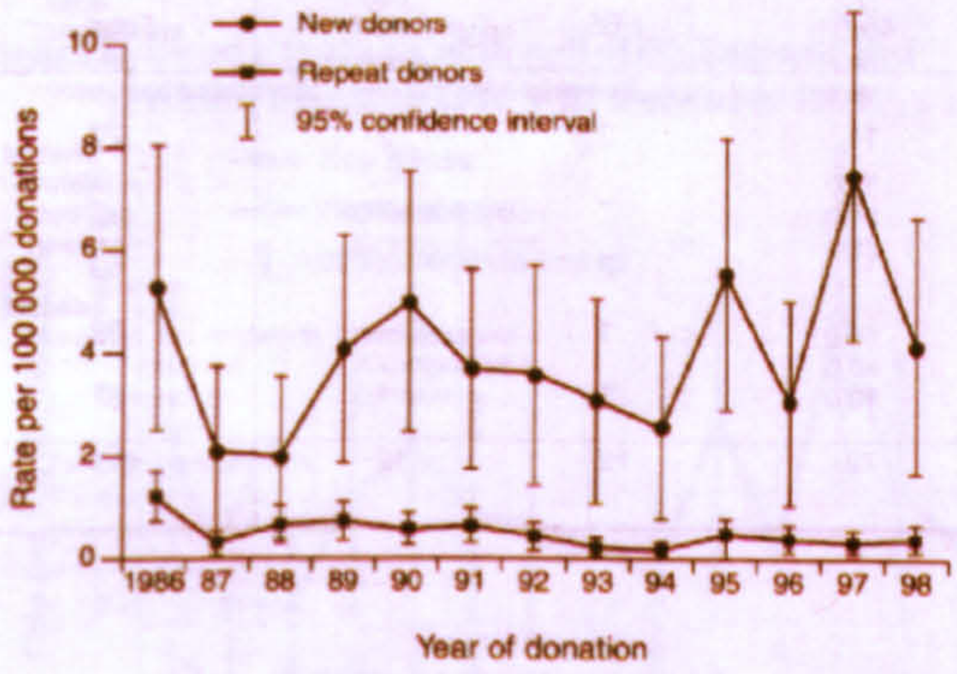


Figure 2 Blood donations with anti-HCV: England and Wales, 1 September 1991 to 31 December 1998

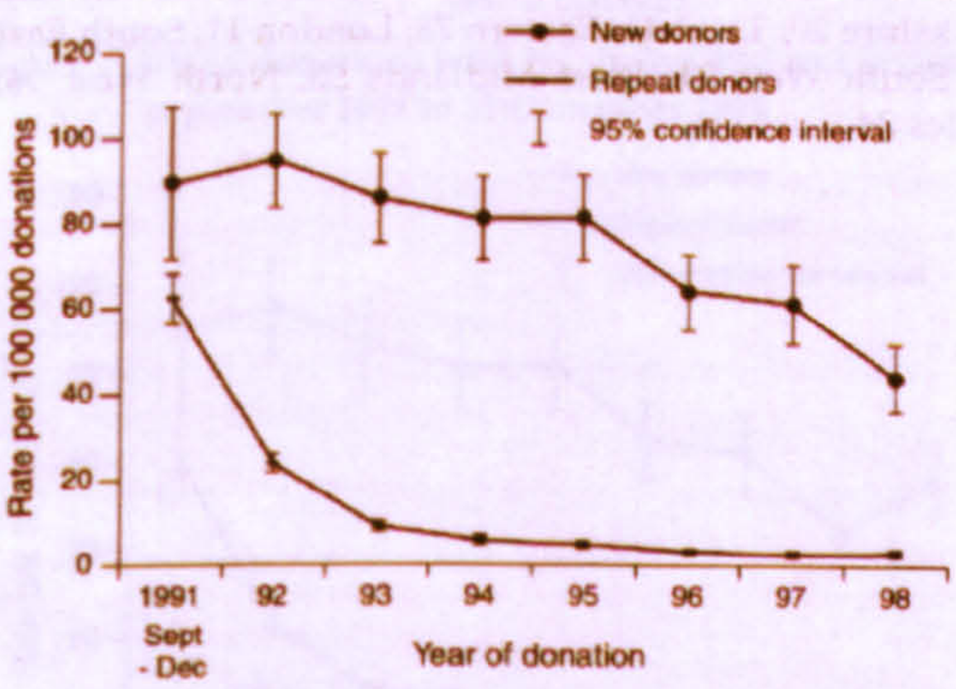
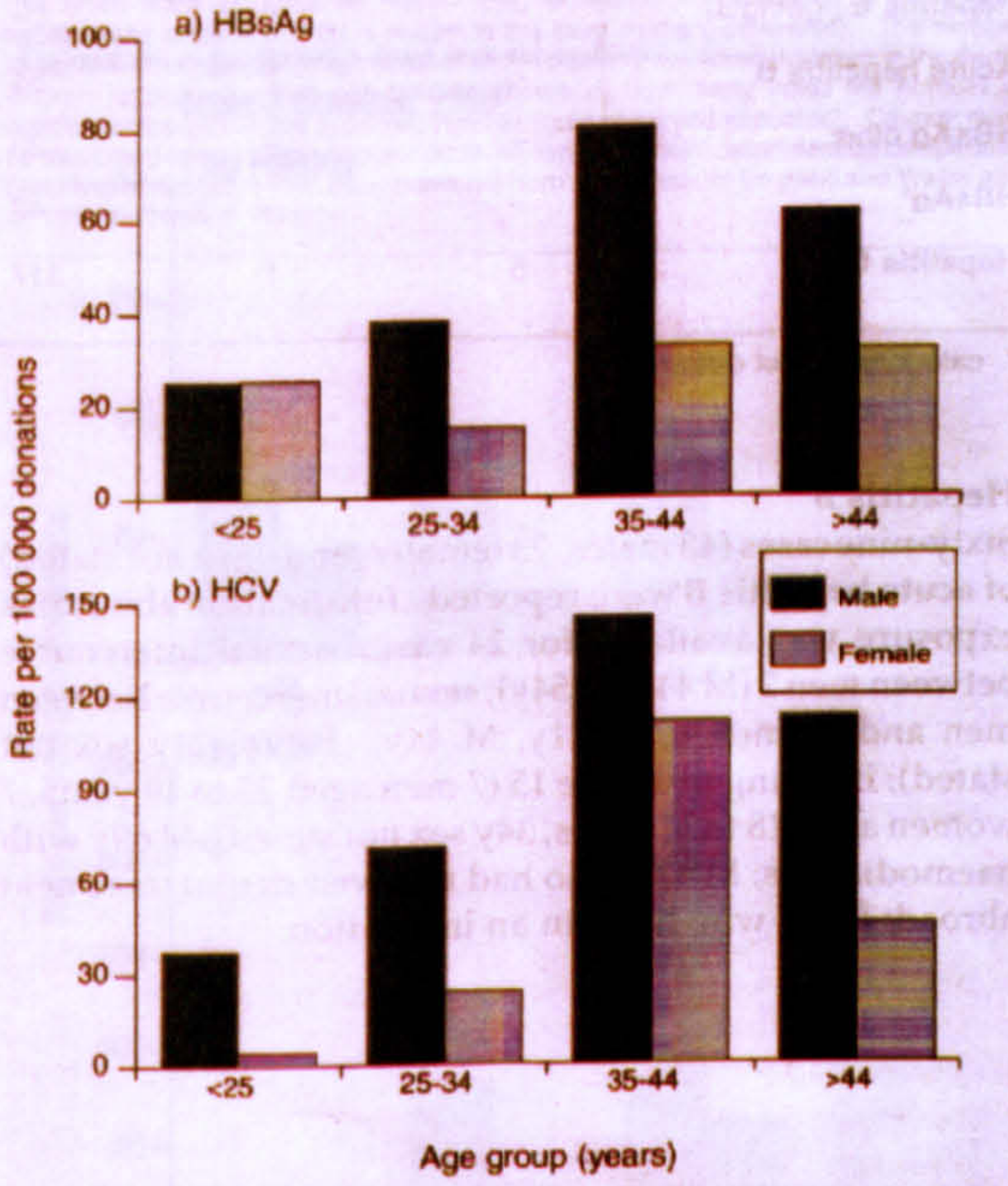


Figure 3 Age group and sex of infected blood donors: newly tested donors, 1998*



* Rates adjusted for underreporting by multiplying the denominator estimate for each age and sex group by the proportion of all detected infections for which information on age and sex has been reported

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Registered as a newspaper.

18 Aug 2000 Communicable Disease Report Vol 10 No 33

Surveillance of viral infections in donated blood: England and Wales, 1999

Donated blood is collected from volunteer adult donors who do not acknowledge any medical conditions, travel history, or behaviours, that are known to be associated with an increased risk of bloodborne infections. During 1999 all blood donations were individually tested for hepatitis B virus surface antigen (HBsAg), hepatitis C virus antibodies (anti-HCV), HIV antibodies (anti-HIV), and treponemal antibodies. Donations are released to the blood supply only if none of these markers of infection are detected. Testing of donated blood for HCV by nucleic acid testing (NAT) began during 1999[1]. Initial testing is performed on pools of donations – positive pools are further tested to identify individual positive donations. Since September 1999, fresh-frozen plasma has only been released if found negative for HCV RNA by NAT. Donors who have any markers of infection detected are informed of their infection, are told to stop donating blood, and are referred to appropriate services for further care. Previous donations from repeat blood donors may not have been tested for some of these markers.

Three hundred and six of 2 559 614 donations (11.95 per 100 000) collected by the English and Welsh blood services during 1999 had markers of viral infections (table). Of these 306 infected donations, 202 (66%) had HCV, 87 (28%) had HBV (including one with dual HCV and HBV infection), and 18 (6%) had anti-HIV. New donors contributed 11% of all blood donations, but 78% of infected donations. Blood donations have been tested for anti-HIV since 1985 and for anti-HCV since 1991. The annual rates of these two markers in donations of blood are shown in figures 1 and 2. The prevalence of HBsAg and of anti-HCV by age group and sex of donors is shown in figure 3.

Table Markers of infection detected in blood donations: England and Wales, 1999

	HBsAg	anti-HCV*	anti-HIV	Any of these three markers†
All donations	87	202	18	306
per 100 000 donations tested	3.40	7.89	0.70	11.95
1 in x donations	29 421	12 671	142 201	8365
Donations from new donors	74	157	9	239
per 100 000 donations tested	25.98	55.13	3.16	83.92
1 in x donations	3849	1814	31 644	1192
Donations from repeat donors‡	13	45	9	67
per 100 000 donations tested	0.57	1.98	0.40	2.95
1 in x donations	174 986	50 551	252 757	33 952

* including one anti-HCV negative repeat donor positive for HCV RNA by NAT
† one new donor had markers of two infections: HBsAg and anti-HCV
‡ may include donations from repeat donors newly tested for markers of infection

Figure 1 Blood donations with anti-HIV: England and Wales, 1 January 1986 to 31 December 1999

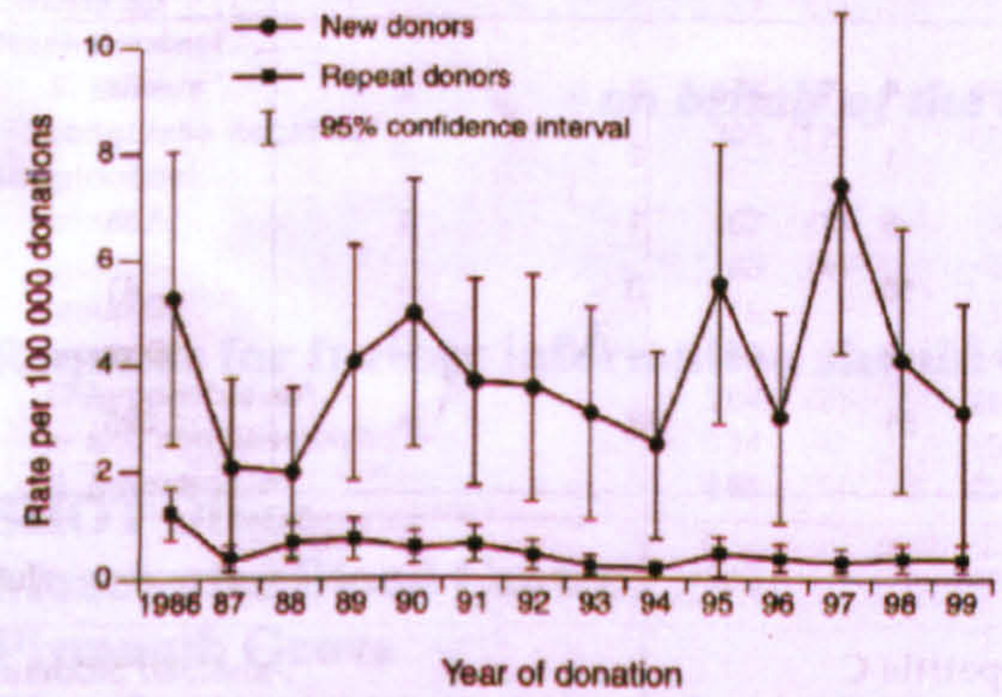
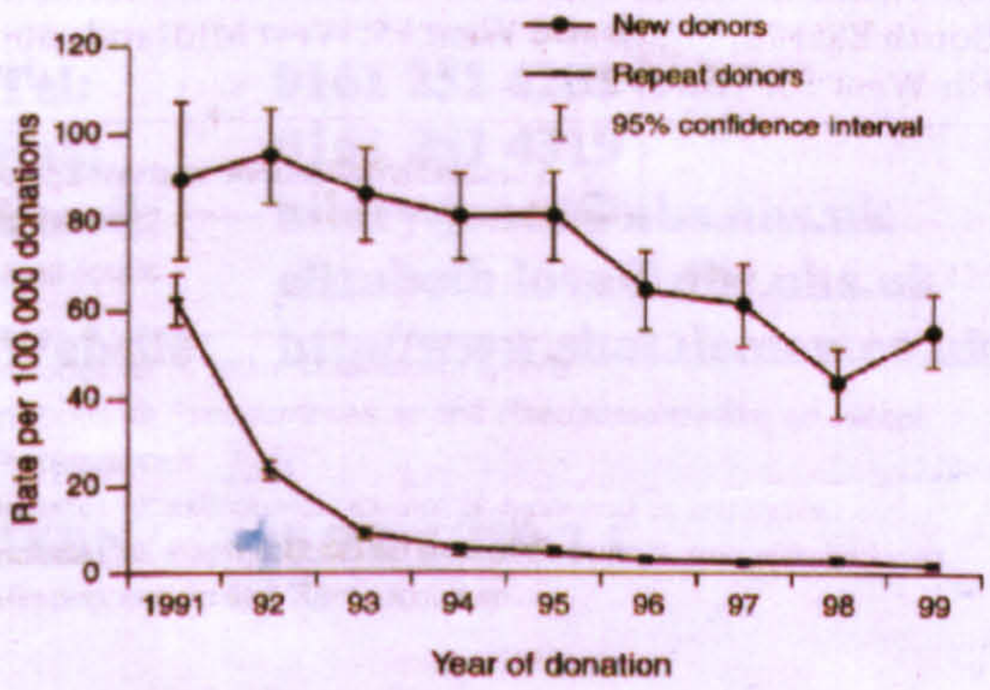


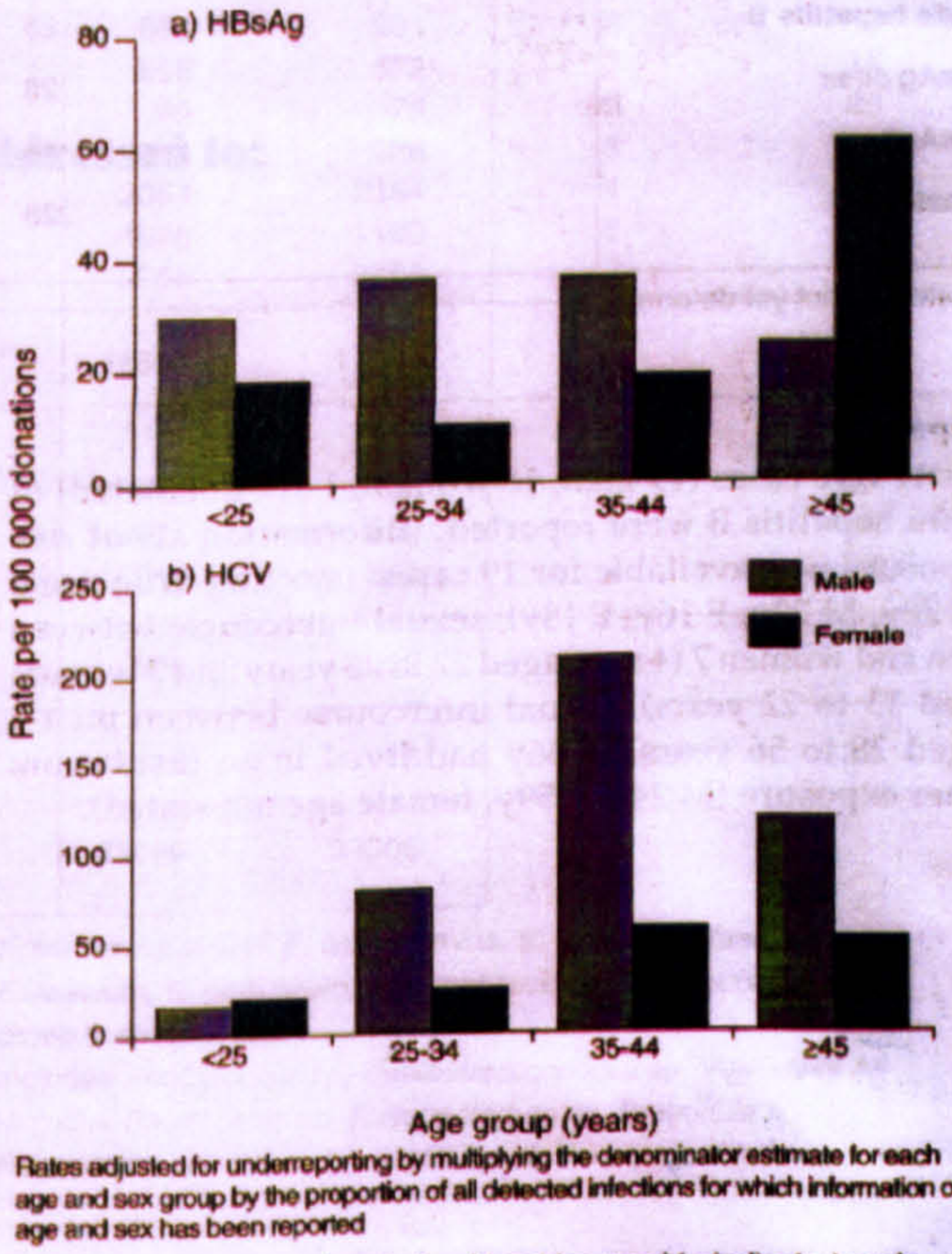
Figure 2 Blood donations with HCV: England and Wales, 1 September 1991 to 31 December 1999



Data are for England and Wales only, unless otherwise stated.

1. Flanagan P, Barbara JAJ. PCR testing of plasma pools: from concept to reality. *Transfus Med Rev* 1999; **13** (3): 164-76.

Figure 3 Age group and sex of infected blood donors: newly tested donors, 1999*



* Rates adjusted for underreporting by multiplying the denominator estimate for each age and sex group by the proportion of all detected infections for which information on age and sex has been reported

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Registered as a newspaper.

Published 7th April, 2000

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ISBN **0 9532 789 2 1**

13. TRANSFUSION-TRANSMITTED INFECTIONS

Introduction

Infectious complications following transfusion differ from non-infectious complications in several ways that may affect the ascertainment and investigation of incidents. The onset of symptoms related to a transfusion-transmitted viral infection may occur from several weeks to years after the date of the transfusion. Reports of infections transmitted by transfusion in a particular year can therefore accrue over the subsequent year(s). The number of cases ascertained by the end of any period is therefore expected to be an incomplete picture of the infections transmitted during that period. Acute infections, such as bacteraemias, that tend to be clinically apparent and diagnosed within days after receipt of the infectious transfusion, may be relatively complete but chronic viral infections will be underrepresented.
In addition, the occurrence of disease, or the observation of serological markers of infection, in individuals who have donated blood can lead to the ascertainment of transfusion-transmitted infections by tracing and testing of recipients exposed to components collected from donors during potentially infectious periods. Recipients may be asymptomatic at this time and only identified by this investigation.
Post-transfusion infections (PTI) may be due to an infected (or contaminated) transfusion or infection may have been acquired from another source. Investigation of markers of infection in an implicated donation, or in subsequent samples from the donors of implicated donations, can confirm transfusion as the probable cause of infection, or identify the need to investigate other possible sources. The blood service must therefore be informed about implicated transfusions so that investigations can be conducted to confirm or refute the suspicion that the implicated transfusion(s) may have been infectious. This is essential to prevent further transmission(s) by other components and/or by chronically infected donors, and to reveal any systematic errors or deficiencies in the blood service testing. Such investigations may involve microbiological testing of many donors and may take several months to complete.

A surveillance system to collect standardised information about infections suspected to have been transmitted by transfusion was introduced in the British Isles (excluding Scotland) and the Republic of Ireland by the National Blood Authority and the Public Health Laboratory Service Communicable Disease Surveillance Centre (PHLS CDSC) in October 1995.

Retrospective data were collated in Scotland for cases occurring in Scotland during this year.

Methods

Participating blood centres (see above) reported all post-transfusion infections of which they had been informed to the NBA/PHLS CDSC infection surveillance system. The criteria for identifying infections eligible for reporting as post-transfusion infections were either:

a) the receipt of the transfusion had been confirmed and the infection in the recipient had been confirmed (by detection of antibody, antigen, RNA/DNA or culture) and there was no evidence that the recipient was infected prior to transfusion, (see exception below) or,

b) the receipt of the transfusion had been confirmed and the recipient had acute clinical hepatitis of no known cause (including no evidence of acute HAV, HBV, HCV, EBV or CMV infection in post-transfusion samples to date).

One category of post-transfusion infections is not included in these data. In January 1999, a meeting of reporters agreed that HCV and HIV infections diagnosed in recipients who had received transfusions in the UK that were not tested for anti-HCV (i.e. pre September 1991) or anti-HIV (i.e. pre October 1985) respectively should be excluded from reporting. The blood service is rarely able to conduct follow-up investigation of donors implicated in these cases and these cases do not contribute to knowledge of the current infection transmission risks of blood transfusions. Numbers and details of such infections are therefore not included in this report.

If other possible sources of infection were known for a post-transfusion infection, an initial report was still requested.

Information about the recipient, the recipient's infection and the transfusion(s) implicated as the possible source of infection formed the basis of the initial report. Subsequently, after appropriate investigations had been completed, details about the findings of the investigation, were reported. (PTI report forms are in Appendix 5)

A post-transfusion infection was classified as a transfusion-transmitted infection if the following criteria were met at the end of the investigation:-

- the recipient had evidence of infection post-transfusion, and there was no evidence of infection prior to transfusion

and, either

- at least one component received by the infected recipient was donated by a donor who had evidence of the same transmissible infection,

or

- at least one component received by the infected recipient was shown to have been contaminated with the agent of infection

Twice this year, all participating blood centres were reminded of the requirement to report, and asked to report any cases that had not yet been notified.

Data received by 31/12/99 about incidents of transfusion-transmitted infections initially reported by blood centres between 1/10/98 and 30/9/99 were included in this report. Data received about incidents reported during the previous three years of the surveillance system are included in a cumulative table.

Unless the investigation was closed due to the identification of a probable source of infection other than transfusion, investigations that were closed without being able to conclusively investigate the source of the post-transfusion infections were classified as post-transfusion infections of undetermined source.

Results

34 initial reports of post-transfusion infections were made by blood centres during the report year. An additional 11 reports were received about post-transfusion reactions that were suspected to be due to bacteria but for which no evidence of bacterial infection (or endotoxin) that could have caused the reaction was sought and found in the recipient or implicated component (i.e. the incidents did not satisfy the criteria for a post-transfusion infection as stated above, but may have been reactions of bacterial origin). Reports were received from 12 of the 21 blood centres participating in the surveillance system. These 12 centres collect approximately 86% of the donations tested by blood centres participating in the surveillance system.

Figure 13 shows the classification of reports during the report year.

Of the 34 post-transfusion infections initially reported by blood centres to the surveillance system between 1/10/98 and 30/9/99, 7 (21%) were classified, after appropriate investigation, as transfusion-transmitted infections. Table 22 shows the transfusion-transmitted infections reported to the surveillance system between 1/10/98 and 30/9/99 by year of transfusion: Four were transfused during the report year, and 3 were transfused prior to the report year.

Figure 13
Classification of post-transfusion infections (and post-transfusion reactions) initially reported between 1/10/98 and 30/9/99.

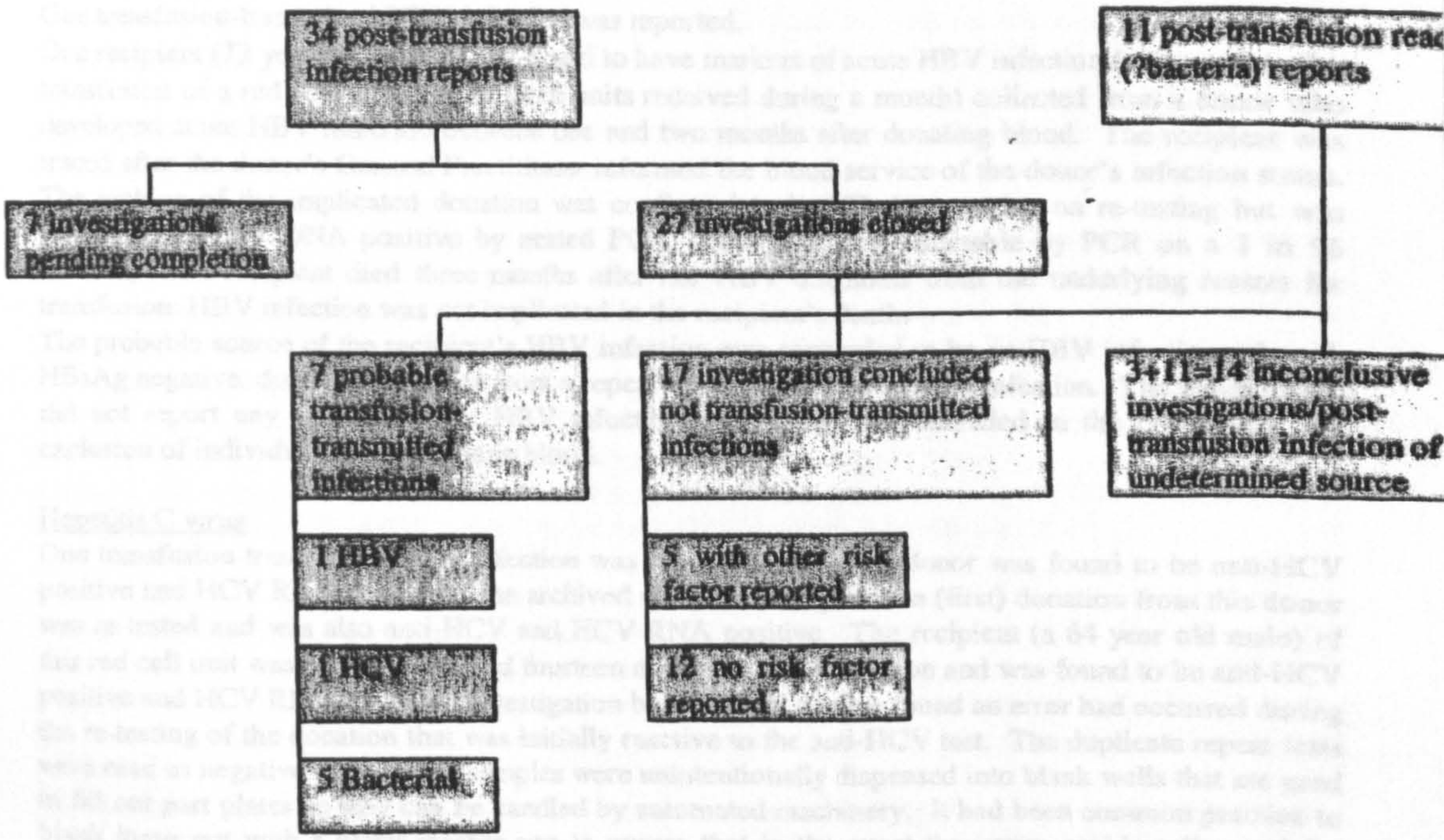


Table 22
Transfusion-transmitted infections reported between 1/10/98-30/9/99 by year of transfusion. The number of incidents are shown, with the total number of identified infected recipients shown in brackets.

Year of transfusion	1997	1998	1999 (to end Sept)	Total
Infection				
HBV	-	1(1)	-	1(1)
HCV	1(1)	-	-	1(1)
Bacteria	-	2(2)[a]	3(3)[a]	5(5)[ax2]
Total[b]	1(1)	3(3)[a]	3(3)[a]	7(7)[ax2]

Notes: [a] Infection was implicated in the death of a recipient.
[b] Additionally, one probable transfusion transmitted bacteraemia (not fatal), transfused during 1998, was reported in Scotland.

A retrospective collation of cases investigated by blood centres in Scotland found three post-transfusion infection investigations during the report year. One recipient (72 year old male) developed pryexia and tachycardia after transfusion with red cells (23 days old, not leucodepleted). The recipient responded to antibiotic therapy and recovered. Coagulase negative *Staphyloccocus* was cultured from the red cell pack. For two post-transfusion HCV infection reports (one transfused in 1996, one in 1999) investigation was completed and no evidence was found to implicate transfusion as the source of infection. A probable source of infection other than transfusion was known for one of these cases.

Details of transfusion-transmitted infections

A. Infections for which donation testing is mandatory

Hepatitis B virus

One transfusion-transmitted HBV infection was reported.

One recipient (73 year old female) was found to have markers of acute HBV infection four months after transfusion of a red cell unit (one of three units received during a month) collected from a donor who developed acute HBV infection between one and two months after donating blood. The recipient was traced after the donor's General Practitioner informed the blood service of the donor's infection status. The archive of the implicated donation was confirmed to be HBsAg negative on re-testing but was found to be HBV DNA positive by nested PCR. (DNA was not detectable by PCR on a 1 in 96 dilution). The recipient died three months after her HBV diagnosis from the underlying reason for transfusion: HBV infection was not implicated in the recipient's death.

The probable source of the recipient's HBV infection was concluded to be an HBV infectious, though HBsAg negative, donation collected from a repeat donor during early acute infection. The blood donor did not report any risk factor for HBV infection that is currently included in the criteria for the exclusion of individuals from donating blood.

Hepatitis C virus

One transfusion-transmitted HCV infection was reported. A repeat donor was found to be anti-HCV positive and HCV RNA positive. The archived sample of the previous (first) donation from this donor was re-tested and was also anti-HCV and HCV RNA positive. The recipient (a 64 year old male) of this red cell unit was traced and tested fourteen months after transfusion and was found to be anti-HCV positive and HCV RNA positive. Investigation by the blood service found an error had occurred during the re-testing of the donation that was initially reactive to the anti-HCV test. The duplicate repeat tests were read as negative because the samples were unintentionally dispensed into blank wells that are used to fill out part plates so they can be handled by automated machinery. It had been common practice to blank these out with a black marker pen to ensure that in the event they were accidentally used for samples they would return a fail safe positive reaction. However new machinery had been introduced which read these as negative. Once the problem was identified corrective and preventative action was put in place to ensure that a different mechanism is used to ensure that blank wells will if accidentally used return a positive result and "fail safe".

The probable source of the recipient's HCV infection was concluded to be an HCV infectious, anti-HCV positive, donation from a new donor. The donation was not excluded from the blood supply because of a laboratory error during the testing process. The blood donor did not report any risk factor for HCV infection that is currently included in the criteria for the exclusion of individuals from donating blood.

HIV

No transfusion transmitted HIV infections were reported during this year.

B. Infections for which donation testing is not mandatory

Bacteria

Five transfusion-transmitted bacteraemias were reported.

One recipient (27 year old male) developed bacteraemia after transfusion with two leucodepleted, 4 day old apheresis platelet units from the same donor. The recipient recovered and was asymptomatic one week after the transfusion. *Staphylococcus epidermidis* was isolated from the platelet packs and from the recipient (and these two isolates had identical banding patterns). *Staph. epidermidis* (with a different DNA fingerprint) was subsequently cultured from swabs of the donor's arms. *Staph. epidermidis* was not grown from swabs taken after standard skin preparation. No failure in the donor arm cleansing procedure at the time of donating the implicated donation had been noted.

The probable source of the recipient's bacteraemia was concluded to be transfusion with platelets contaminated with skin flora from the donor's arm.

One recipient (52 year old male) suffered a severe febrile reaction during transfusion of a leucodepleted, 3 day old apheresis platelet unit, and died later the same afternoon. On inspection the next day the remainder of the platelet pack had some signs of bacterial contamination (unusual orange colouration and small specks visible when held up to the light). *Escherichia coli* was cultured from the recipient's blood and from the platelet pack (and these two isolates had identical biochemical profiles). No leaks or defects were identified in the platelet pack. An interview with the donor confirmed absence of symptoms of infection at and around the time of donation and swabs of the donor's arm skin were negative on culture.
The probable source of the recipient's reaction, and cause of death, was concluded to be transfusion with platelets contaminated with *E.coli*. No source of the contamination was identified.

One recipient (78 year old female) suffered symptoms including feeling hot, sweaty and dyspnoeic during transfusion of a pooled, leucodepleted, 4 day old platelet unit. The recipient subsequently recovered and was completely asymptomatic two weeks after the transfusion. Blood cultures were not taken from the recipient. *Staphylococcus epidermidis* was cultured from the platelet pack and from the red cell unit made from the same donation.
An interview with the donor confirmed absence of symptoms of infection at and around the time of donation and swabs from the skin of the donor's arm were negative on culture.
The probable source of the recipient's transient reaction was concluded to be transfusion with platelets contaminated with *Staph. epidermidis*. No source of the contamination was identified.

One recipient (63 year old female) developed urticaria, rigors and pyrexia during transfusion of a pooled, leucodepleted, 4 day old platelet unit. The recipient was pyrexial for three days after transfusion and was treated with broad spectrum antibiotics. *Bacillus cereus* was cultured from the recipient's blood and from the platelet pack (and these two isolates were both of type 29). *B cereus* (type 29) was also cultured from swabs from the skin of the donor's arm (both pre- and post- arm cleansing).
The probable source of the recipient's reaction was concluded to be transfusion with platelets contaminated with *B. cereus* from the donor's arm.

N.B. The above four cases were associated with leucocyte depleted platelets: all platelets issued in the UK since January 1999 have been leucocyte depleted. The numbers of cases are too small to detect any effect of leucodepletion on bacterial contamination of components.

One recipient (58 year old female) suffered a respiratory and cardiac arrest during transfusion of a second unit of red cells (33 day old, not leucodepleted) and died the same day. *Yersinia entercolitica* (serotype 09, biotype 3) was isolated from the patient's blood, the implicated red cell pack, the archive of the implicated donation and a fresh sample of blood taken from the donor 5 months after the donation. On follow-up the donor reported a history of diarrhoea a few weeks prior to the donation.
The probable source of the recipient's reaction, and cause of death, was concluded to be transfusion with red cells contaminated with *Yersinia entercolitica* from the donor's blood.

Details of post-transfusion infections not found to be transfusion-transmitted infections

Three (9%) post-transfusion infections (all bacteraemias) were classified as post-transfusion infections of undetermined source due to inconclusive investigation of the transfusion(s) implicated as the source of infection. For seventeen (50%) post-transfusion infection reports (1 HAV infection, 5 HBV infections, 7 HCV infections, 2 HIV infections, 1 syphilis infection and 1 bacteraemia), investigation was completed and no evidence was found to implicate transfusion as the source of infection. A possible source of infection other than transfusion was known for 5 of these infections (HBVx1: invasive medical procedure abroad, HCVx1: renal dialysis & transplant, HCVx1: tattoo, HIVx2: sexual risk factors).

Reporting delay

For the 5 transfusion-transmitted bacterial infections, disease occurred on the same day as the transfusion. Both of the transfusion-transmitted viral infections (1 HBV and 1 HCV) were diagnosed with sub-clinical infections (130 days and 440 days after transfusion respectively) during the follow up of suspected infectious donations. Blood centres were informed of the bacteraemias suspected to be associated with transfusion on the same day (3 cases), the next day, and 7 days after transfusion. The intervals between the blood centre being informed and the completion of the initial surveillance report form (i.e. reporting delay) were 124 days, 98 days, 32 days, 22 days and 12 days for the 5 clinically detected (bacterial) infections. The average interval between transfusion and the initial report (i.e. including all time intervals and reporting delays) was 135 days (n=7).

Under-reporting

The cases ascertained by this surveillance system were diagnosed, suspected to be attributable to transfusion, communicated to the blood service, and reported by a blood centre to the surveillance centre. At any one of these steps, other post-transfusion infections may have been missed and the extent of under-reporting of post-transfusion infections is therefore unknown. The proportion of post-transfusion infections that are reported each year may vary as other factors such as testing performed on transfusion recipients, awareness of transfusion as a possible source of infection, reporting of information to blood centres and reporting of information from blood centres to the surveillance centre vary.

Previous year

During the previous reporting year (i.e. 1/10/97 to 30/9/98) 4 transfusion-transmitted infections were reported (see SHOT Annual Report 1997-98 for details of these cases). One of these was an HCV infection transmitted by transfusion prior to anti-HCV testing of blood donations: this case has now been excluded from the cumulative figures. None of the post-transfusion infections reported during the 1997-98 year that were pending full investigation at the time of the last (i.e. 1997-98) SHOT annual report have been subsequently concluded to have been transfusion-transmitted infections.

The investigations of seven post-transfusion infections that were classified as pending full investigation in the 1997-98 SHOT report have subsequently been concluded to be not due to transfusion (4 cases) or inconclusive (3 cases). One of the inconclusive cases concerned an HIV infection in a patient who had received multiple transfusions during the early 1990s and had no other risk factors for HIV infection. Investigation of the transfusions given to this patient did not identify a source of infection, however, as not all transfusions were investigated, transfusion with HIV infectious, anti-HIV tested, blood was concluded to be the probable, although unproven, source of infection.
Table 23 shows the cumulative number of transfusion-transmitted infections reported by the end of September 1999.
Figure 14 shows the number of reports received by year of transfusion since October 1995.

Table 23
Cumulative total transfusion-transmitted infections: reported between 1/10/95-30/9/99 by date of transfusion. The number of incidents is shown with the total number of identified infected recipients in brackets.

Year of transfusion	pre-1995	1995	1996	1997	1998	1999 (to end Sept)-	Total	Deaths
Infection								
HAV	-	-	1(1)	-	-	-	1(1)	
HBV	1(1)[b]	1(1)	1(1)	1(1)	1(1)-		5(5)	
HCV	-	-	1(1)	1(1)	-		2(2)	
HIV[c]	-	-	1(3)	-	-	-	1(3)	
Bacteria	-	1(1)	1(1)	3(3)	3(3)[ax2]	3(3)[a]	11(11)	3
Malaria	-	-	-	1(1)[a]	-	-	1(1)	1
Total[d]	1(1)[b]	2(2)	5(7)	6(6)[a]	4(4)[ax2]	3(3)[a]	21(23)	4

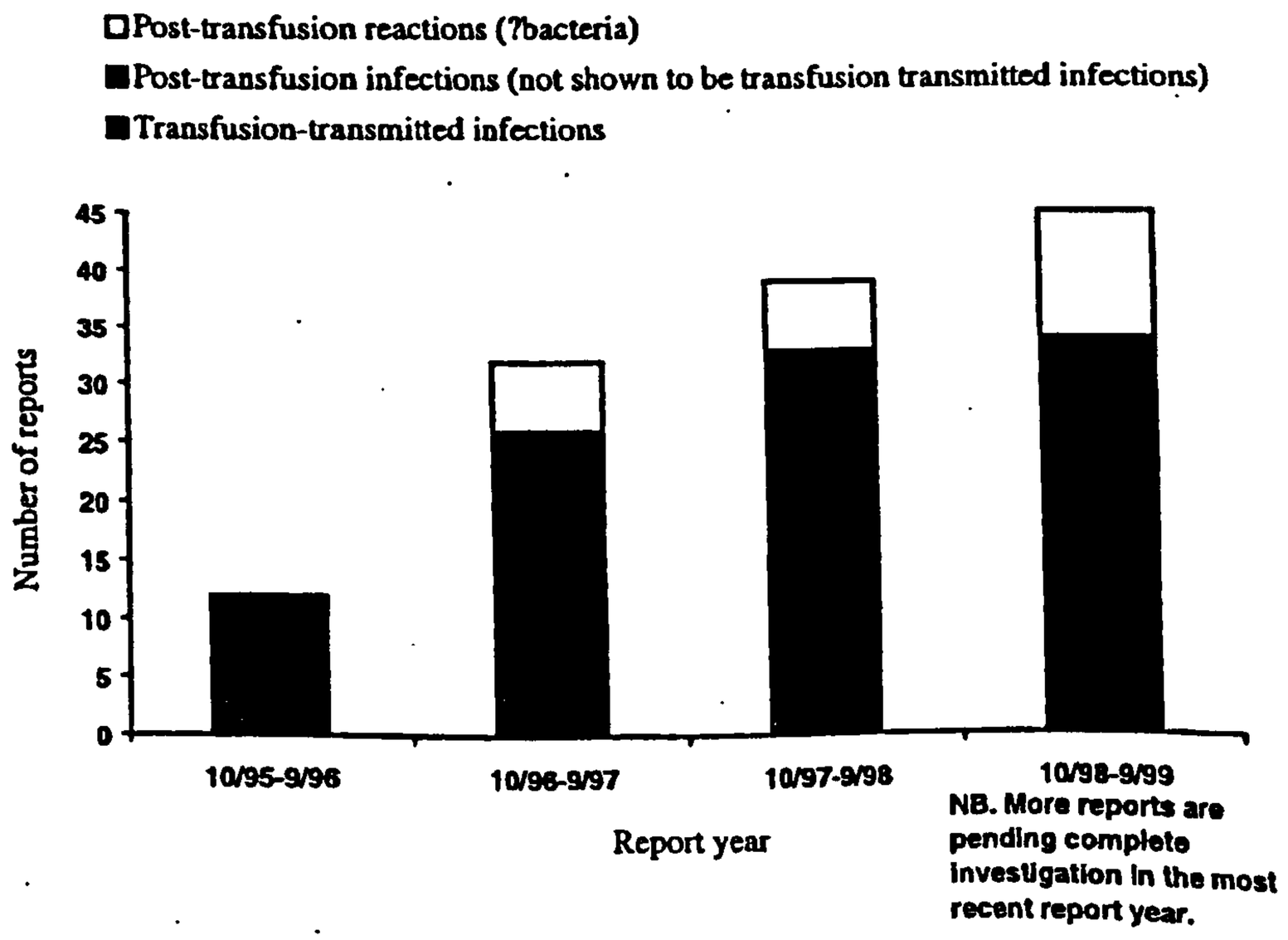
Notes: [a] Infection was implicated in the death of a recipient.

[b] One household member who was caring for the recipient has been diagnosed with acute HBV.

[c] One additional investigation, initially reported during 97-98 and concluded during 98-99, failed to confirm or refute transfusion transmission of HIV infection during the early 1990s. As the patient had received multiple transfusions, and had no other risk factors for infection, transfusion with HIV infectious blood was concluded to be the probable, although unproven, source of infection.

[d] Additionally, one probable transfusion transmitted bacteraemia (not fatal), transfused during 1998, was reported in Scotland.

Figure 14
PTI reports by report year



COMMENTARY

- Reported transfusion-transmitted infections are rare: only 7 confirmed cases were recognised during this 12-month period of reporting. Investigations of a further 29 cases of post-transfusion infection were reported. 50% of the PTI reports during this year have been shown not to be caused by transfusion. For 9% of the reports the investigation was inconclusive and for the remainder investigation continues. Similarly, in Scotland during this year, one probable case was recognised and two reports were shown not to be caused by transfusion.

- Eleven cases of post-transfusion reactions suspected (but not confirmed) to be due to bacteria were also reported. Conclusive investigation of a suspected bacteraemia in a transfusion recipient relies heavily on the collection and handling of relevant samples at the hospital where the transfusion was performed. This means that absence of evidence of an infection, or toxin, in donations given to recipients who had post-transfusion reactions that were suspected, on clinical presentation, to be due to bacteria does not equate with evidence of absence of a transfusion-transmitted infection or toxin.

- The intervals between transfusion and diagnosis of transfusion-transmitted infections were long - many weeks, months or years. Infections transmitted by transfusion between 1/10/98 and 30/9/99 will continue to be ascertained by the surveillance system as diagnoses are made in the future.

- Two transfusion-transmitted viral infections (1 HBV and 1 HCV) were detected by follow-up of recipients after the detection of infections in blood donors. In one case (HCV) the donor's infection was diagnosed by the blood service by the testing of a subsequent donation, and in the other case (HBV) the donor's GP informed the blood service of the donor's infection. Neither of these transfusion-transmitted infections had caused symptomatic, diagnosed disease in the recipients. One of these transfusion-transmitted infections (HBV) was due to a donation collected from a donor during the marker negative "window period" early in a recent infection. One (HCV) was due to a laboratory error resulting in a false negative test result. Neither of these donors reported risk factors.

- Five transfusion-transmitted bacterial infections arose from donations from donors with infections for which no routine microbiology testing is performed.

- One reported transfusion-transmitted infection resulted from errors in the microbiological testing, or release, of blood donations.

- Two transfusion-transmitted infections, both bacterial, reported during this year resulted in the death of the recipient.

- Several reports have been received of components that were observed to have visual signs of bacterial contamination before use, were not transfused, were sent for bacteriological investigation and were found to contain bacteria expected to cause disease in a recipient if transfused. Inspection of components, especially platelets, detected contamination and prevented morbidity in these incidents. Such inspection should continue to be encouraged. These reports indicate "near-miss" bacterial transmissions. The investigation of the source of the contamination in these cases can be as informative as the investigation of transmissions, and the possibility of requesting and collating some information about these cases in the future is being considered.

RECOMMENDATIONS

- Careful inspection of blood components can, in some cases, detect bacterial contamination and prevent potential transmission. Components showing any unusual colour, turbidity or clumping should not be transfused, but should be returned to the Hospital Blood Bank for culture.

- Clinicians should report all post-transfusion infections diagnosed in their patients to their regional blood service for appropriate investigation. Blood centres should, in turn, complete an initial report form as soon as possible.

- The quality of investigation of transfusion reactions suspected to be due to bacteria is variable. Hospitals should consult guidelines and the blood service about the investigation of such cases, including the sampling and storage of implicated units. National guidelines (from the NBS) on the investigation of these cases are currently being revised following comments from users.

- Donors' clinicians (and donors themselves) can aid the detection of transfusion-transmitted infections, and hence their appropriate care, by communicating with the blood service about any relevant history of blood donation on patients diagnosed with blood borne infections.

- National collation of data arising from these cases needs to continue over several years before a picture of the extent and nature of the infectious complications of transfusion can emerge.